TRANSMITTAL OF APPEAL BRIEF

Docket No.
SON-2047

In re Application of: Akihiko Koh et al.

Application No.	Filing Date	Examiner	Group Art Unit
09/802,857-Conf. #3304	March 12, 2001	M. J. Yigdall	2122

Invention: DATA PROCESSING APPARATUS

TO THE COMMISSIONER OF PATENTS:

Transmitted herewith is the Appeal Brief in this application, with respect to the Notice of Appeal filed: February 22, 2005 .

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47,255 (Brian Dutton) Dated: April 22, 2005

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Docket No.: SON-2047
(80001-2047)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Akihiko KOH et al.

Confirmation No.: 3304

Application No.: 09/802,857

Art Unit: 2122

Filed: March 12, 2001

Examiner: M. J. Yigdall

For: DATA PROCESSING APPARATUS PERFORMING PREDETERMINED DATA PROCESSING IN ACCORDANCE WITH INSTRUCTION CODES READ FROM A PROGRAM MEMORY STORING A PROGRAM (as amended)

APPELLANT'S BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
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Dear Sir:

INTRODUCTORY COMMENTS

This is an Appeal Brief under 37 C.F.R. §41.37 appealing the final decision of the Examiner dated November, 19, 2004. Each of the topics required by 37 C.F.R. §41.37 is presented herewith and is labeled appropriately.

This brief is in furtherance of the Final Office Action on November, 19, 2004.

A Notice of Appeal has been filed in this case on February 22, 2005.

I. REAL PARTY IN INTEREST

Sony Corporation of Tokyo, Japan ("Sony") is the real party in interest of the present application. An assignment of all rights in the present application to Sony was executed by the inventor and recorded by the U.S. Patent and Trademark Office at **reel 011655, frame 0005.**

II. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

Claims 1-12 (canceled);

Claims 13-25 (rejected).

IV. STATUS OF AMENDMENTS

Subsequent to the final rejection of November, 19, 2004, no Amendment has been filed.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention relates to a data processing apparatus, for example, a data processing apparatus including at least a central processing unit (CPU) and a memory providing programs for the CPU, which is able to correct bugs in the programs stored in the memory after manufacture.

Figure 3 depicts a CPU 10, a memory (ROM) 30, a serial interface (SIO) 40, a memory (RAM) 50, buses (including a data bus and an address bus) 60, and a debugging circuit 100 (Specification at page 15, lines 6-15).

As shown within figure 7, the debugging circuit 30 has a plurality of bug address setting registers 100-1, 110-2 and a plurality of coincidence detecting circuits 120-1, 120-2 (Specification at page 24, lines 14-16).

One of the plurality of bug address setting registers 100-1, 110-2 hold one of a plurality of bug addresses BADR0-1, BADR0-2 that show the start of a buggy part of the program stored in the program memory 30 (Specification at page 24, lines 17-20).

One of a plurality of coincidence detecting circuits 120-1, 120-2 compares a program address for reading instruction codes from the program memory 30 with the one of the plurality of bug addresses held in the one of the plurality of bug address setting registers 100-1, 110-2. In addition, one of the plurality of coincidence detecting circuits 120-1, 120-2 output one of a plurality of coincidence signals S_{A1}, S_{A2} when the program address and the one of the plurality of bug addresses BADR0-1, BADR0-2 coincide (Specification at page 24, lines 21-24).

Another of the plurality of bug address setting registers 100-1, 110-2 hold another of a plurality of bug addresses BADR0-1, BADR0-2 that show the start of a buggy part of the program stored in the program memory 30 (Specification at page 24, lines 17-20).

Another of a plurality of coincidence detecting circuits 120-1, 120-2 compares a program address for reading instruction codes from the program memory 30 with another of the plurality of bug addresses held in another of the plurality of bug address setting registers 100-1, 110-2. In addition, another of the plurality of coincidence detecting circuits 120-1, 120-2 output another of a plurality of coincidence signals S_{A1}, S_{A2} when the program address and another of the plurality of bug addresses BADR0-1, BADR0-2 coincide (Specification at page 24, lines 21-24).

The central processing unit 10 receives the plurality of coincidence signals S_{A1}, S_{A2} (Specification at page 25, lines 4-6). Upon receiving the plurality of coincidence signals S_{A1}, S_{A2},

the central processing unit 10 executes one of a plurality of debugging programs stored within random access memory 50 when the one of the plurality of coincidence signals S_{A1}, S_{A2} indicates a coincidence of the program address and the one of the plurality of bug addresses BADR0-1, BADR0-2, and executes another of a plurality of debugging programs stored within random access memory 50 when the another of the plurality of coincidence signals S_{A1}, S_{A2} indicates a coincidence of the program address and the another of the plurality of bug addresses BADR0-1, BADR0-2 (Specification at page 25, lines 15-19). The central processing unit 10 executes the program stored within the program memory 30 when the plurality of coincidence signals S_{A1}, S_{A2} indicates a non-coincidence of the program address and any of the plurality of bug addresses BADR0-1, BADR0-2 (Specification at page 20, lines 8-14 and page 24, lines 7-13).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issue presented for consideration in this appeal is as follows:

Whether the Examiner erred in rejecting claims 13-25 under 35 U.S.C. §103 as allegedly being unpatentable over U.S. Patent No. 5,454,100 to Sagane in view of U.S. Patent No. 5,701,506 to Hosotani.

This issue will be discussed hereinbelow.

VII. ARGUMENT

In the Final Office Action of November, 19, 2004:

The Examiner erred in rejecting claims 13-25 under 35 U.S.C. §103 as allegedly being unpatentable over Sagane in view of Hosotani.

For at least the following reasons, Appellant submits that these rejections are both technically and legally unsound and should therefore be reversed.

Grouping of claims

Claims 13-25 are currently pending and finally rejected in this application, with claim 3 being independent. For purposes of the issues presented by this appeal:

Claims 13-18 and 21-25 stand or fall together.

Claim 19 stands or falls alone.

Claim 20 stands or falls alone.

The arguments set forth in the following section provide reasons why these claims are considered patentable, 37 C.F.R. §41.37(c)(1)(vii).

The Examiner erred in rejecting claims 13-25 under 35 U.S.C. §103 as allegedly being unpatentable over Sagane in view of Hosotani.

This rejection is traversed at least for the following reasons.

The Patent and Trademark Office (PTO) has the burden of showing a prima facie case of obviousness. *In re Bell*, 991 F.2d 781, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). In determining the propriety of the Patent Office case for prima facie obviousness, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the proposed substitution or other modification. *In re Taborsky*, 502 F.2d 775, 780-81, 183 USPQ 50, 55 (CCPA 1974). Moreover, *prima facie* obviousness of a claimed invention is established only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

Claims 13-18 and 21-25

Claim 13 and the claims dependent thereon include the features of:

a debugging circuit having a plurality of bug address setting registers and a plurality of coincidence detecting circuits,

one of said plurality of bug address setting registers holding one of a plurality of bug addresses that show the start of a buggy part of said program stored in said program memory,

one of said plurality of coincidence detecting circuits comparing a program address for reading instruction codes from said program memory with said one of said plurality of bug addresses held in said one of said plurality of bug address setting registers, said one of said plurality of coincidence detecting circuits outputting one of a plurality of coincidence signals when said program address and said one of said plurality of bug addresses coincide,

another of said plurality of bug address setting registers holding another of said plurality of bug addresses that show the start of another buggy part of the program stored in the program memory,

another of said plurality of coincidence detecting circuits comparing said program address for reading instruction codes from said program memory with said another of said plurality of bug addresses held in said another of said plurality of bug address setting registers, said another of said plurality of coincidence detecting circuits outputting another of said plurality of coincidence signals when said program address and said another of said plurality of bug addresses coincide; and

a central processing unit receiving said plurality of coincidence signals, wherein said central processing unit:

executes one of a plurality of debugging programs stored within random access memory when said one of said plurality of coincidence signals indicates a coincidence of said program address and said one of said plurality of bug addresses,

executes another of said plurality of debugging programs stored within said random access memory when said another of said plurality of coincidence signals indicates a coincidence of said program address and said another of said plurality of bug addresses, and

executes said program stored within said program memory when said plurality of coincidence signals indicates a non-coincidence of said program address and any of said plurality of bug addresses.

Sagane arguably teaches an electronic apparatus. Figure 1 is a block diagram of the *first embodiment* of Sagane, while figure 3 of Sagane is a block diagram of the *second embodiment* of Sagane.

The claimed invention includes a debugging circuit having a plurality of bug address setting registers and a plurality of coincidence detecting circuits.

Regarding the first embodiment of Sagane, the Office Action fails to show within the first embodiment of Sagane where the feature of a debugging circuit having a plurality of bug address setting registers and a plurality of coincidence detecting circuits is to be found (Sagane at figure 1). Thus, all claimed features are absent from within the first embodiment of Sagane.

Instead, the Office Action relies upon the second embodiment for the claimed debugging circuit. Specifically, the Office Action contends that the second embodiment of Sagane provides for a plurality of comparators or coincidence detection circuits (Office Action at page 3).

In response to this contention, all claimed features are absent from within the second embodiment of Sagane, either individually or in combination with the first embodiment, at least for the following reasons.

The claimed invention additionally includes a central processing unit receiving said plurality of coincidence signals.

The second embodiment of Sagane arguably teaches a single central processing unit (CPU) 2, a single comparator 8, a single correction address register 21 and a single correction data register 22. Moreover, the second embodiment of Sagane arguably teaches that pluralities of comparators 8, correction address registers 21 and correction data registers 22 may be provided to address the multiple bugs (Sagane at figure 3, column 7, lines 1-3).

Nevertheless, the Office Action *admits* that the second embodiment of Sagane *fails* to disclose, teach or suggest the CPU 2 as receiving said plurality of coincidence signals (Office Action at page 8). Thus, all claimed features are absent from within the second embodiment of Sagane.

As a gap filler, the Office Action contends that it would have been apparent to the skilled artisan that the plurality of comparators would output corresponding plurality of coincidence signals (Office Action at page 8).

In response to this contention, the second embodiment of Sagane fails to expressly state that each of the pluralities of comparators 8 described at column 7, line 1 of Sagane would necessarily output a coincidence signal. But even if each of the pluralities of comparators 8 described at column 7, line 1 of Sagane would necessarily output a coincidence signal, the Office Action fails to clearly identify within the second embodiment of Sagane where and how the CPU 2 is to receive a plurality of coincidence signals, since signal A of comparator 8 found within figure 3 is applied to switch 23 and not to the CPU 2. Thus, all claimed features are absent from within the second embodiment of Sagane.

The Office Action refers to the first embodiment of Sagane. In response, the teachings found within a single prior art reference can render a claim obvious. *Sibia Neurosciences Inc. v. Cadus Pharmaceutical Corp.*, 225 F.3d 1349, 1355-56, 55 USPQ2d 1927, 1931 (Fed. Cir. 2000). But when obviousness is based on a particular prior art reference, there *must* be a showing of a

suggestion or motivation to modify the teachings of *that reference*. *B.F. Goodrich Co. v. Aircraft Braking Systems Corp.*, 72 F.3d 1577, 1582, 37 USPQ2d 1314, 1318 (Fed. Cir. 1996).

At least for the following reasons, there is no showing of a suggestion or motivation that would lead the skilled artisan to apply the first embodiment of Sagane for the purpose of modifying the teachings of the second embodiment of Sagane.

Specifically, the first embodiment of Sagane arguably depicts a comparator 8 that supplies the interrupt control circuit 7d with a coincidence signal E via the switch 7c, thereby generating an interrupt (Sagane at figure 1, column 5, lines 13-17). However, the Office Action fails to show where and how the CPU 2 for first embodiment of Sagane is to receive a plurality of coincidence signals. Thus, claimed features that are absent from within the second embodiment of Sagane are also absent from within the first embodiment of Sagane.

The Office Action contends that figure 1 of Sagane teaches the coincidence signal being connected to the CPU 2 (Office Action at page 3). In response, the first embodiment of Sagane arguably depicts the presence of a coincidence signal E (Sagane at figure 1, column 3, line 49). Yet, figure 1 of Sagane fails to disclose, teach or suggest the coincidence signal E being connected to the CPU 2. Instead, the comparator 8 for the first embodiment of Sagane supplies the interrupt control circuit 7d with a coincidence signal E via the switch 7c (Sagane at figure 1, column 5, lines 13-15).

The Office Action contends that the access switching unit 7 provides the interrupt for signaling coincidence (Office Action at page 4). However, the first embodiment of Sagane fails to show where and how the CPU 2 is to receive an interrupt. Thus, claimed features that are absent from within the second embodiment of Sagane are also absent from within the first embodiment of Sagane.

Additionally, while the first embodiment of Sagane may arguably depict some sort of linkage between the CPU 2 and the interrupt control circuit 7d (Sagane at figure 1), and while the first embodiment of Sagane arguably teaches that the interrupt handling effected by the interrupt control circuit 7d transfers control to the address given by an interrupt vector register 7b (Sagane at

column 3, lines 61-63), the first embodiment of Sagane fails to disclose, teach or suggest that an interrupt signal is provided from the interrupt control circuit 7d to the CPU 2. Thus, claimed features that are absent from within the second embodiment of Sagane are also absent from within the first embodiment of Sagane.

But even if the first embodiment of Sagane teaches that an interrupt signal is provided from the interrupt control circuit 7d to the CPU 2, and even if the first embodiment of Sagane suggests a plurality of coincidence signals E, the first embodiment of Sagane fails to disclose, teach or suggest the execution of a debugging program when one of the coincidence signals indicates a coincidence of the program address and the one of the plurality of bug addresses, along with the execution of another debugging program when another of the coincidence signals indicates a coincidence of the program address and the another of the plurality of bug addresses.

For example, the first embodiment of Sagane arguably teaches the presence of an interrupt vector register 7b (Sagane at figure 1). And the first embodiment of Sagane arguably teaches that the start address of the correction content stored in the RAM 4 is latched in the interrupt vector register 7b at the time of correction data writing (Sagane at column 3, lines 63-65). Yet, the first embodiment of Sagane fails to disclose, teach or suggest either a plurality of start addresses stored within either the RAM 4 or a plurality of start addresses stored within the interrupt vector register 7b. Thus, claimed features that are absent from within the second embodiment of Sagane are also absent from within the first embodiment of Sagane.

The Office Action contends that the skilled artisan would have been motivated to substitute the switch 23 found within the second embodiment of Sagane with the access switching unit 7 found within the first embodiment of Sagane (Office Action at page 10).

In response to this contention, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the claimed substitution or other modification. *In re Lalu and Foulletier*, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984). In addition, "it is impermissible, however, simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting

elements from references to fill the gaps. The references themselves must provide some teaching whereby the applicant's combination would have been obvious" (citations omitted). *In re Gorman*, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). In this regard, the Office Action fails to provide some motivation as to why the skilled artisan would have made this alleged substitution or other modification.

Additionally, Sagane arguably teaches that another modification of the second embodiment is to interpose the control flag switch 7a and switch 7c of figure 1 between the comparator 8 and the switch 23 in figure 3 (Sagane at column 7, lines 3-6). However, nowhere within Sagane is there found a disclosure, teaching or suggestion for the incorporation of the interrupt control circuit 7d, as associated with the first embodiment of Sagane, into the block diagram of the second embodiment of Sagane.

The assertions made within the Office Action amount to nothing more than an "obvious-to-try" situation. Specifically, "an 'obvious-to-try' situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued." *In re Eli Lilly & Co.*, 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990). Moreover, "an invention is 'obvious to try' where the prior art gives either no indication of which parameters are critical or no direction as to which of many possible choices is likely to be successful." *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 806, 10 USPQ2d 1843, 1845 (Fed. Cir. 1989).

All claimed features are absent from the first and second embodiments of Sagane, either individually or as a whole since the cited prior art does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued. "Obvious to try" is not the standard under §103. *In re O'Farrell*, 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988).

The Office Action cites Hosotani for the features deficient within Sagane. Hosotani arguably teaches microcomputer having ROM program that can be altered. Within Hosotani the

first to third match circuits 9a-9c are connected to a three-input OR circuit 14. Hosotani arguably teaches that the output of OR circuit 14 is applied to switch 10 (Hosotani at figures 2, 6, 8, 10, 11) or to ROM 17 (Hosotani at figures 7, 12). Yet, Hosotani fails to disclose, teach or suggest the output of OR circuit 14 being applied to CPU 1. Thus, Hosotani fails to disclose, teach or suggest a central processing unit receiving a plurality of coincidence signals.

Thus, Sagane and Hosotani, either individually or as a whole, fail to disclose, teach or suggest the features found within the claimed invention.

Claim 19

In addition to the reasons provided hereinabove with respect to claim 13, the rejection of claim 19 is traversed at least for the following reasons.

Within claim 19, the central processing unit receives the plurality of coincidence signals as separate interrupt requests. However, the Office Action *admits* that the second embodiment of Sagane *fails* to disclose, teach or suggest the CPU 2 as receiving said plurality of coincidence signals (Office Action at page 8). Moreover, the CPU 2 receiving a plurality of coincidence signals as separate interrupt requests is also absent from the first embodiment of Sagane. In addition, Hosotani fails to disclose, teach or suggest a central processing unit receiving a plurality of coincidence signals.

Thus, Sagane and Hosotani, either individually or as a whole, fail to disclose, teach or suggest the features found within the claimed invention.

Claim 20

In addition to the reasons provided hereinabove with respect to claim 13, the rejection of claim 20 is traversed at least for the following reasons.

Within claim 20, the central processing unit receives the plurality of coincidence signals as a single interrupt request. However, the Office Action *admits* that the second embodiment of

Sagane *fails* to disclose, teach or suggest the CPU 2 as receiving said plurality of coincidence signals (Office Action at page 8). Moreover, the CPU 2 receiving a plurality of coincidence signals as separate interrupt requests is also absent from the first embodiment of Sagane. In addition, Hosotani fails to disclose, teach or suggest a central processing unit receiving a plurality of coincidence signals.

Thus, Sagane and Hosotani, either individually or as a whole, fail to disclose, teach or suggest the features found within the claimed invention.

Conclusion

The claims are considered allowable for the same reasons discussed above, as well as for the additional features they recite. Reversal of the Examiner's decision is respectfully requested.

Dated: April 22, 2005

Respectfully submitted,

By_____

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CLAIMS APPENDIX

1-12. (canceled)

13. (previously presented) A data processing apparatus performing predetermined data processing in accordance with instruction codes read from a program memory storing a program, the data processing apparatus comprising:

a debugging circuit having a plurality of bug address setting registers and a plurality of coincidence detecting circuits,

one of said plurality of bug address setting registers holding one of a plurality of bug addresses that show the start of a buggy part of said program stored in said program memory,

one of said plurality of coincidence detecting circuits comparing a program address for reading instruction codes from said program memory with said one of said plurality of bug addresses held in said one of said plurality of bug address setting registers, said one of said plurality of coincidence detecting circuits outputting one of a plurality of coincidence signals when said program address and said one of said plurality of bug addresses coincide,

another of said plurality of bug address setting registers holding another of said plurality of bug addresses that show the start of another buggy part of the program stored in the program memory,

another of said plurality of coincidence detecting circuits comparing said program address for reading instruction codes from said program memory with said another of said plurality of bug addresses held in said another of said plurality of bug address setting registers, said another of said plurality of coincidence detecting

circuits outputting another of said plurality of coincidence signals when said program address and said another of said plurality of bug addresses coincide; and

a central processing unit receiving said plurality of coincidence signals, wherein said central processing unit:

executes one of a plurality of debugging programs stored within random access memory when said one of said plurality of coincidence signals indicates a coincidence of said program address and said one of said plurality of bug addresses,

executes another of said plurality of debugging programs stored within said random access memory when said another of said plurality of coincidence signals indicates a coincidence of said program address and said another of said plurality of bug addresses, and

executes said program stored within said program memory when said plurality of coincidence signals indicates a non-coincidence of said program address and any of said plurality of bug addresses.

14. (previously presented) A data processing apparatus as set forth in claim 13, wherein an interrupt request for said central processing unit is generated when any of said plurality of coincidence signals indicates a coincidence of said program address and any of said plurality of bug addresses.

15. (previously presented) A data processing apparatus as set forth in claim 14, wherein, when said one of said plurality of coincidence signals indicates said coincidence of said program address and said one of said plurality of bug addresses, said central processing unit:

suspends execution of said program stored within said program memory after receiving said interrupt request,

processes an instruction stored within said random access memory at said one of said plurality of bug addresses to begin execution of said one of a plurality of debugging programs after suspending execution of said program,

suspends execution of said one of a plurality of debugging programs by processing an instruction residing within said one of a plurality of debugging programs that has a return address, and

resumes execution of said program stored within said program memory by processing an instruction residing within said program memory at said return address.

16. (previously presented) A data processing apparatus as set forth in claim 14, wherein, when said another of said plurality of coincidence signals indicates said coincidence of said program address and said another of said plurality of bug addresses, said central processing unit:

suspends execution of said program stored within said program memory after receiving said interrupt request,

processes an instruction stored within said random access memory at said another of said plurality of bug addresses to begin execution of said another of a plurality of debugging programs after suspending execution of said program,

suspends execution of said another of a plurality of debugging programs by processing an instruction residing within said another of a plurality of debugging programs that has a return address, and

resumes execution of said program stored within said program memory by processing an instruction residing within said program memory at said return address.

17. (previously presented) A data processing apparatus as set forth in claim 14, wherein said plurality of bug addresses is stored within said random access memory.

18. (previously presented) A data processing apparatus as set forth in claim 13, wherein said plurality of coincidence signals is a plurality of interrupt request signals.

19. (previously presented) A data processing apparatus as set forth in claim 13, wherein said central processing unit receives said plurality of coincidence signals as separate interrupt requests.

20. (previously presented) A data processing apparatus as set forth in claim 13, wherein said central processing unit receives said plurality of coincidence signals as a single interrupt request.

21. (previously presented) A data processing apparatus as set forth in claim 20, wherein said plurality of coincidence signals are logically AND'ed together and input to said central processing unit as an interrupt request signal.

22. (previously presented) A data processing apparatus as set forth in claim 13, wherein said plurality of debugging programs are input during initialization into said random access memory from a source external to said data processing apparatus.

23. (previously presented) A data processing apparatus as set forth in claim 13, wherein said random access memory stores a plurality of interrupt vectors of start addresses, said start addresses identifying memory areas within said random access memory that contain said plurality of debugging programs.

24. (previously presented) A data processing apparatus as set forth in claim 13, wherein said central processing unit suspends an instruction being executed and reads an instruction code from a program address designated by a predetermined address table when said central processing unit executes any of said plurality of debugging programs stored within random access memory.

25. (previously presented) A data processing apparatus as set forth in claim 13, wherein said program memory is read only memory.

EVIDENCE APPENDIX

1. *Sibia Neurosciences Inc. v. Cadus Pharmaceutical Corp.*, 225 F.3d 1349, 1355-56, 55 USPQ2d 1927, 1931 (Fed. Cir. 2000).

2. *B.F. Goodrich Co. v. Aircraft Braking Systems Corp.*, 72 F.3d 1577, 1582, 37 USPQ2d 1314, 1318 (Fed. Cir. 1996).

3. *In re Bell*, 991 F.2d 781, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993).

4. *In re Gorman*, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991).

5. *In re Eli Lilly & Co.*, 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990).

6. *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 806, 10 USPQ2d 1843, 1845 (Fed. Cir. 1989).

7. *In re O'Farrell*, 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988).

8. *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

9. *In re Lalu and Foulletier*, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984).

10. *In re Taborsky*, 502 F.2d 775, 780-81, 183 USPQ 50, 55 (CCPA 1974).

Sibia Neurosciences Inc. v. Cadus Pharmaceutical Corp.

U.S. Court of Appeals Federal Circuit
55 USPQ2d 1927

Decided September 6, 2000
No. 99-1381

Headnotes

PATENTS

1. Patentability/Validity -- Obviousness -- Relevant prior art -- Particular inventions (§ 115.0903.03)

Patentability/Validity -- Obviousness -- Evidence of (§ 115.0906)

Claimed cell-based screening method for identification of compounds that exhibit agonist and antagonist activity with respect to particular cell surface proteins is obvious in view of prior art scientific paper, since only difference between experiments described in reference and those claimed in patent is that in reference, compounds are known to interact with cell surface proteins, whereas in asserted claim they are not, since express teaching in prior art was that cells having heterologous surface proteins, such as those in prior art reference, were ideal candidates for use in drug screening methods, since undisputed testimony was that reference provided "straightforward functional assay" for determining response of heterologous cell surface protein when exposed to particular compound, and since, given nature of problem addressed, these teachings provide motivation to modify cells of reference to be used with unknown compounds.

Particular patents -- Chemical -- Cell-based screening method

5,401,629, Harpold and Brust, assay methods and compositions useful for measuring the transduction of an intracellular signal, invalid.

Case History and Disposition:

Appeal from the U.S. District Court for the Southern District of California, Gonzales, J.

Action by Sibia Neurosciences Inc. against Cadus Pharmaceutical Corp. for patent infringement. Defendant appeals from jury verdict in favor of plaintiff and assessment of $18 million in damages. Reversed; Mayer, C.J., dissenting in separate opinion.

Attorneys:

Stephen P. Swinton, Anthony M. Stiegler, J. Christopher Jaczko, Kent M. Walker, and Amy S. Hellenkamp, of Cooley Godward, San Diego, Calif., for plaintiff-appellee.

Laura A. Coruzzi and S. Leslie Misrock, of Pennie & Edmonds, New York, N.Y.; Stanton T. Lawrence III, Paul J. Zegger, and Carl P. Bretscher, of Pennie & Edmonds, Washington, D.C., for defendant-appellant.

Judge:

Before Mayer, chief judge, and Michel and Gajarsa, circuit judges.

Opinion Text

Opinion By:

Gajarsa, J.

Cadus Pharmaceutical Corporation ("Cadus") appeals the judgment of the United States District Court for the Southern District of California entered after a jury verdict finding the patent claims at issue infringed and not invalid, and assessing damages of $18 million. Because we determine that the asserted claims are obvious as a matter of law, we reverse.

BACKGROUND

The identification of compounds that bind with particular cell surface proteins is useful in the search for new drugs. When such binding occurs, a cascade of biochemical events is activated within the cell in which a linkage, known as a signal transduction pathway, is formed between the cell surface protein and a gene in the cell's DNA. This linkage allows the cell to respond to signals from the external environment, which is critical for the cell to properly function. Compounds that activate this linkage often prove useful in pharmaceutical applications because many diseases stem from the malfunctioning of cellular communications.
In general, when a compound activates a signal transduction pathway, the cell responds by directing the production or non-production of a protein from a responsive gene in the DNA.

Protein production involves two distinct processes--transcription and translation. Transcription refers to the process by which a strand of messenger RNA ("mRNA") is created by the expression of a gene. Translation refers to the process by which a corresponding protein (i.e., a sequence of amino acids) is created from the mRNA. Compounds that trigger or enhance transcription and translation are referred to as agonists, and compounds that block or decrease such activity are called antagonists. The displaying of agonist and antagonist activity is an indication that a

compound has bound with the cell surface protein and has activated the signal transduction pathway.

SIBIA Neurosciences, Inc. ("SIBIA") is the owner of U.S. Patent No. 5,401,629 ("the '629 patent"), which is directed to a cell-based screening method useful for the identification of compounds that exhibit agonist and antagonist activity with respect to particular cell surface proteins. According to the patent, the claimed methods are particularly effective because they allow a scientist to rapidly and reliably screen large numbers of compounds for agonist and antagonist activity. *See* '629 patent, col. 1, ll. 45-50. Thus, the scientist could quickly develop a list of candidate compounds that merit further in-depth studies for therapeutic applications. *See id.* Claim 1, the only independent claim, reads as follows:

1. A method for identifying compounds that modulate cell surface protein-mediated activity by detecting intracellular transduction of a signal generated upon interaction of the compound with the cell surface protein, comprising:

comparing the amount of transcription of a reporter gene or the amount of reporter gene product expressed in a first recombinant cell in the presence of the compound with the amount of transcription or product in the absence of the compound, or with the amount of transcription or product in a second recombinant cell; and

selecting compounds that change the amount of transcription of a reporter gene or the amount of reporter gene product expressed in the first recombinant cell in the presence of the compound compared to the amount of transcription or product in the absence of the compound, or compared to the amount of transcription or product in the second recombinant cell, wherein: the cell surface protein is a surface receptor or ion channel; the first recombinant cell contains a

reporter gene construct and expresses the cell surface protein; the second recombinant cell is identical to the first recombinant cell, except that it does not express the cell surface protein; and the reporter gene construct contains:

(a) a transcriptional control element that is responsive to the intracellular signal that is generated by the interaction of an agonist with the cell surface protein; and

(b) a reporter gene that encodes a detectable transcriptional or translational product and that is in operative association with the transcriptional control element.

See id. , col. 13, l. 44 - col. 14, l. 12.

The methods claimed in the '629 patent utilize a recombinant cell that is exposed to various compounds in order to determine whether those compounds exhibit the desired activity. This recombinant cell, in addition to the host cell itself, has two basic components: a heterologous 1 cell surface protein and a reporter gene construct. The cell surface protein can be either an ion channel or a cell surface receptor. Ion channels are proteins that act as pores in the cell membrane and allow small inorganic ions to flow in or out of the cell. These ion channels open and close based on interaction with certain external compounds. Cell surface receptors, on the other hand, are proteins that span the external membrane of the cell and bind with particular molecules to commence a chain of intracellular reactions that transmit external signals to the DNA. As described above, cell surface proteins are physiologically important because they play a vital role in the stimulation of signal transduction pathways, and thus, the cell's ability to respond appropriately to stimuli from the external environment.

The second major component of the cell utilized in the '629 patent is the reporter gene construct, which consists of a transcriptional control element and a reporter gene. The transcriptional control element is a gene that reacts to the signal from the cell surface protein and regulates transcription of the reporter gene. The reporter gene, through the processes of transcription and translation, creates a corresponding protein, referred to as "reporter gene product." Both transcription of the reporter gene and translation to the reporter gene product can be measured. In the claimed methods, this recombinant cell is used in a battery of assays, the goal of which is to determine if a given compound exhibits the desired binding activity with respect to a particular cell surface protein. The method of claim 1 contains two assays. In the first assay, referred to as the "compound/no compound assay," the recombinant cell is exposed to a test compound. The amount of reporter gene transcription, or

reporter gene product expressed in that recombinant cell, is then compared to the amount of reporter gene transcription or reporter gene product expressed in a recombinant cell that was not exposed to the test compound. In the second assay, known as the "receptor/no receptor assay," two recombinant cells are exposed to a test compound. However, one of the recombinant cells has a cell surface protein, but the other does not. The amount of reporter gene transcription or reporter gene product expressed in both of these cells is then compared. Based on these measurements, the scientist is able to detect whether the compound has bound to the cell surface protein and modulated the signal transduction pathway. This, in turn, allows the scientist to determine whether the compound is a candidate for further study, or should be excluded from consideration.

SIBIA sued Cadus for infringement of the '629 patent. The court held a *Markman* hearing, *see Markman v. Westview Instruments, Inc.* , 52 F.3d 967, 979, 34 USPQ2d 1321, 1329 (Fed. Cir. 1995) (en banc), *aff'd* , 517 U.S. 370 [38 USPQ2d 1461] (1996), and issued an order construing numerous claim terms, including "identifying compounds," "cell," "recombinant cell," "comparing the amount," "identical" and "selecting compounds." Only the construction of "cell," "identifying compounds," and "selecting compounds" are relevant to this appeal. Before the district court, Cadus argued that because the claims use the term "cell" without modification, this term should refer to all cells, eukaryotic as well as prokaryotic. 2 Alternatively, Cadus argued that if "cell" should be limited to less than *all* cells, it should be limited to only mammalian cells, because the examples found in the written description of the patent only discuss mammalian cells. The court decided, however, that because the patentee describes the cells used in the claimed methods as "eukaryotic cells" in the written description, *see* '629 patent, col. 3, ll. 52-56, col. 4, ll. 9-11, a person of ordinary skill in the art would interpret cell as found in the claim language to mean only eukaryotic cells.

Also important to this appeal is the court's construction of the phrases "identifying compounds" and "selecting compounds." At the *Markman* hearing, the parties disagreed as to whether this claim language required the compounds to be unknown to interact with the particular cell surface protein prior to conducting the assays, or whether these terms include both compounds known and unknown to interact with the cell surface proteins. The court held that the ordinary meaning of "identifying compounds" is determining which compounds interact with a particular

cell surface protein from a group of compounds with unknown properties. Thus, the testing of compounds that are known to interact with a particular cell surface protein does not fall within the ambit of "identifying compounds." Similarly, the court held that "selecting compounds" referred only to choosing compounds from a group previously unknown to interact with a cell surface protein based on the results of the reporter gene transcription and translation analyses. The case then proceeded to a jury trial. At trial, Cadus asserted that the claims of the '629 patent were invalid as obvious under 35 U.S.C. Section 103(a) or as not enabled under Section 112, Para. 1. With regard to obviousness, Cadus asserted that the claims of the '629 patent would have been obvious in view of Deborah J. Stumpo et al., *Identification of c-fos Sequences Involved in Induction by Insulin and Phorbol Esters* , 263 J. Biological Chem. 1611 (Feb. 1988) ("Stumpo") alone, given the knowledge in the art as embodied in the review article by Henry A. Lester, *Heterologous Expression of Excitability Proteins: Route to More Specific Drugs?* , 241 Science 1057 (Aug. 1988) ("Lester"). Additionally, Cadus asserted that the claims would have been obvious in view of Stumpo in combination with William S. Chen et al., *Requirement for intrinsic protein tyrosine kinase in the immediate and late action of the EGF receptor* , 328 Nature 820 (Aug. 1987) ("Chen"), and Ronald Mark Evans et al., *Hormone Receptor Compositions and Methods* , WO 88/03168 (May 1988) ("Evans"). With regard to non-enablement, Cadus claimed that if "cell" is to be interpreted to broadly include all eukaryotic cells, the claims are not enabled because the written description discloses only how to practice the invention using mammalian cells. The jury returned a verdict in favor of SIBIA, finding that Cadus infringed claims 1, 2, 4-7, 9, 10, 12, and 14 of the '629 patent. The jury rejected Cadus's invalidity defenses of obviousness and non-enablement. Damages, based on the calculation of a "reasonable royalty," were assessed at $18 million. Cadus filed numerous post-trial motions, including motions for judgment as a matter of law ("JMOL") or a new trial on the issues of infringement and invalidity, and motions for

remittitur or a new trial for damages. All of Cadus's motions were denied. This appeal followed.

DISCUSSION A. Standard of Review

We review the denial of a motion for JMOL following a jury verdict by reapplying the district

court's standard of review. *See* *Tec Air, Inc. v. Denso Mfg.* , 192 F.3d 1353, 1357, 52 USPQ2d 1294, 1296 (Fed. Cir. 1999). Thus, we review issues of law *de novo* . With regard to factual findings, we must presume that the jury resolved all factual disputes in favor of the prevailing party, and we must leave those findings undisturbed as long as they are supported by substantial evidence. *See* *Jurgens v. McKasy* , 927 F.2d 1552, 1557, 18 USPQ2d 1031, 1035 (Fed. Cir. 1991).

A factual finding is supported by substantial evidence if a reasonable jury could have found in favor of the prevailing party in light of the evidence presented at trial. *See* *Tec Air* , 192 F.3d at 1358, 52 USPQ2d at 1296; *see also* *Consolidated Edison Co. v. NLRB* , 305 U.S. 197, 229 (1938) ("Substantial evidence is more than a mere scintilla. It means such relevant evidence as a reasonable mind might accept as adequate to support a conclusion."). Thus, substantial evidence review involves an examination of the record as a whole, taking into consideration evidence that both justifies and detracts from the decision of the fact-finder. *See* *In re Gartside* , 203 F.3d 1305, 1312, 53 USPQ2d 1769, 1773 (Fed. Cir. 2000); *National Presto Indus., Inc. v. West Bend Co.* , 76 F.3d 1185, 1192, 37 USPQ2d 1685, 1690 (Fed. Cir. 1996) (holding that a jury verdict must be sustained if it is supported by substantial evidence based on a review of the entirety of the record). In reviewing the record, we must draw all reasonable inferences in favor of the prevailing party, and not make credibility determinations or substitute our view of the conflicting evidence for that of the jury. *See* *Connell v. Sears, Roebuck & Co.* , 722 F.2d 1542, 1546, 220 USPQ 193, 197 (Fed. Cir. 1983). If, however, after reviewing all of the evidence in a light most favorable to the prevailing party, this court is convinced that a reasonable jury could not have found in that party's favor, we must reverse the denial of JMOL.

B. Obviousness

The first step in any invalidity analysis is claim construction, an issue of law that this court reviews *de novo* . *See* *Cybor Corp. v. FAS Techs., Inc.* , 128 F.3d 1448, 1456, 46 USPQ2d 1169, 1174 (Fed. Cir. 1998) (en banc). In this appeal, the key issues of claim construction are largely undisputed. As described in more detail above, the method of claim 1 utilizes a recombinant cell having both a heterologous cell surface protein and a reporter gene construct. This cell is used in two assays--the compound/no compound assay and the receptor/no receptor assay--in which compounds are "identified" and "selected." Neither party disputes that

the terms "identifying compounds" and "selecting compounds" limit the claimed method to identifying and selecting compounds that are not previously known to interact with a particular cell surface protein. The only remaining claim construction issue on appeal is the proper interpretation of the term "cell." According to Cadus, the court erred by limiting "cell" to only eukaryotic cells, as opposed to all cells, both eukaryotic and prokaryotic. SIBIA defends the district court's interpretation by pointing to certain passages in the written description that, it asserts, support the district court's narrower claim construction. *See Comark Communications, Inc. v. Harris Corp.* , 156 F.3d 1182, 1186, 48 USPQ2d 1001, 1005 (Fed. Cir. 1998) (discussing the "fine line" between reading a claim in light of the written description and reading a limitation into the claim from the written description). However, because we decide that the claim is obvious even under the district court's narrow construction of the term "cell," we need not decide whether the court erroneously imported the "eukaryotic" limitation into the claim, or simply interpreted the claim in light of the specification. Thus, we can proceed to the question of obviousness accepting the district court's construction of claim 1.

A patent claim is invalid "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. Section 103(a) (1994). While the ultimate conclusion of obviousness is for the court to decide as a matter of law, several factual inquiries underlie this determination. *See Graham v. John Deere Co.* , 383 U.S. 1, 17-18 [148 USPQ 459] (1966). These inquiries include the scope and content of the prior art, the level of ordinary skill in the field of the invention, the differences between the claimed invention and the prior art, and any objective evidence of non-obviousness such as long-felt need, and commercial success. *See id.* Because an issued

patent is presumed valid, there must be clear and convincing evidence supporting the obviousness determination. *See Kahn v. General Motors Corp.* , 135 F.3d 1472, 1480, 45 USPQ2d 1608, 1614 (Fed. Cir. 1998). While the presentation at trial of a reference that was not before the examiner does not change the presumption of validity, the alleged infringer's burden may be more easily carried because of this additional reference. *See Applied Materials, Inc. v. Advanced Semiconductor Materials Am., Inc.* , 98 F.3d 1563, 1569, 40 USPQ2d 1481, 1485

(Fed. Cir. 1996).

On appeal, Cadus argues that the Stumpo reference alone, which was not before the PTO examiner, is sufficient to invalidate the patent under Section 103, given the level of skill in the art at the time of the invention. In appropriate circumstances, a single prior art reference can render a claim obvious. *See, e.g., B.F. Goodrich Co. v. Aircraft Braking Sys. Corp.* , 72 F.3d 1577, 1582, 37 USPQ2d 1314, 1318 (Fed. Cir. 1996); *In re O'Farrell* , 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). However, there must be a showing of a suggestion or motivation to modify the teachings of that reference to the claimed invention in order to support the obviousness conclusion. *See B.F. Goodrich* , 72 F.3d at 1582, 37 USPQ2d at 1318. This suggestion or motivation may be derived from the prior art reference itself, *see O'Farrell* , 853 F.3d at 902, 7 USPQ2d at 1680, from the knowledge of one of ordinary skill in the art, or from the nature of the problem to be solved. *See Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.* , 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed. Cir. 1996); *see also Motorola, Inc. v. Interdigital Tech. Corp.* , 121 F.3d 1461, 1472, 43 USPQ2d 1481, 1489 (Fed. Cir. 1997) (" [T]he suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art."). Determining whether there is a suggestion or motivation to modify a prior art reference is one aspect of determining the scope and content of the prior art, a fact question subsidiary to the ultimate conclusion of obviousness. *See Tec - Air, Inc.* , 192 F.3d at 1359, 52 USPQ2d at 1298 (stating that the factual underpinnings of obviousness include whether a reference provides a motivation to combine its teachings with another). Because the jury returned a verdict in favor of SIBIA, we must presume that all factual disputes, such as the motivation to modify, were resolved in its favor. *See Jurgens* , 927 F.2d at 1557, 18 USPQ2d at 1035.

The parties are in general agreement regarding the teachings of the Stumpo paper itself. Stumpo describes recombinant cells engineered to have both a heterologous cell surface receptor and a responsive reporter gene construct. These cells are identical to the recombinant cells used in the claimed methods. Stumpo describes using these cells in a transcription-based assay in order to detect cell surface receptor activation. According to the unrebutted testimony of Dr. Struhl, the Stumpo paper described a "straightforward functional assay" for analyzing the response of a particular cell surface protein in the presence of a compound. However, these transcription-based assays use the compound insulin, which was known to interact with the surface receptors of Stumpo's recombinant cells. The purpose of these assays was not drug

screening, but the characterization of certain aspects of the genetic material of the recombinant cell. Claim 1 of the '629 patent, on the other hand, claims a method using recombinant cells identical to Stumpo's in transcription-based assays with compounds not previously known to interact with the cell surface protein of the recombinant cell. The only difference between the experiments described in the Stumpo paper and claim 1 is that in the Stumpo paper, the compounds are known to interact with the cell surface proteins, while in claim 1, they are not. Thus, we must presume that the jury determined that there was no motivation to modify the Stumpo reference such that the cells described therein would be utilized with compounds that were not previously known to interact with the cell surface proteins. *See id.* We hold that this key factual finding is not supported by substantial evidence.

[1] As discussed above, the motivation to modify a reference can come from the knowledge of those skilled in the art, from the prior art reference itself, or from the nature of the problem to be solved. *See In re Rouffet* , 149 F.3d 1350, 1358, 47 USPQ2d 1453, 1458 (Fed. Cir. 1998). The undisputed evidence indicates that there was a motivation to modify Stumpo. It was known in the art at the time of the invention that cells with heterologous cell surface proteins were ideal candidates for drug screening methods. The Lester review article describes the widespread use of such cells in the identification of new drugs:

A new approach for a systematic program to develop more specific drugs has simultaneously occurred to several investigators. This approach is based on the

expression of excitability molecules 3 from DNA clones in cells that readily support such expression and can readily be studied with the full range of modern physiological and pharmacological techniques.

Lester, 241 Science at 1058. Lester goes on to describe that drug screening methods utilizing the expression of excitability molecules (i.e., cell surface receptors) can overcome the "highly empirical approach to the design of drugs" and the lack of functional assays for determining which compounds act on which cell surface receptors. *Id.* at 1062. These are the identical problems that were being addressed by the '629 patent. *See* '629 patent, col. 1, ll. 36-44 ("The availability of rapid, effective means to identify compounds which interact with . . . cell surface-localized receptors would enable the rapid screening of a large number of compounds to

identify those candidates suitable for further in-depth studies of therapeutic applications."). Similarly, the prior art Dull patent (U.S. Patent No. 4,859,609) teaches a drug screening method using cells that had a cell surface receptor. Thus, the express teaching in the prior art was that cells having heterologous cell surface proteins, a characteristic found in the Stumpo cells, have been successfully used in drug screening methods and were, in fact, ideal candidates for such use. Additionally, the undisputed testimony was that Stumpo provided a "straightforward functional assay" for determining the response of the heterologous cell surface protein when exposed to a compound. Given that the nature of the problem was the development of rapid and effective drug screening methods based on the response of a heterologous cell surface protein, these teachings provide the motivation to modify Stumpo.

In response to these teachings, SIBIA merely points out that the cells described in the Lester article and the Dull patent are not described as having reporter gene constructs like those used in the '629 patent and found in the Stumpo cells. SIBIA, however, is confusing obviousness with anticipation. It is true that these references do not contain an express teaching to use a cell identical to that taught by Stumpo in a drug screening method. It is equally true that these references, particularly Lester, teach that cells with heterologous cell surface receptors were known in the art to have been successfully used in drug screening methods and that the Stumpo cells have such heterologous cell surface receptors. SIBIA's response, that Lester does not mention cells that contain a reporter gene construct in addition to the heterologous cell surface receptor, is to no avail absent some evidence that this additional characteristic would have made such a cell a less attractive candidate for drug screening methods. *See* *In re Gurley* , 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994) (" [A] reference will teach away if it suggests that the line of development flowing from the reference's disclosures is unlikely to be productive of the result sought by the applicant."). SIBIA makes no allegation of a teaching away in Lester. To the contrary, the evidence is unrebutted that cells with reporter gene constructs were also known in the art to be useful in drug screening methods. *See* U.S. Patent No. 5,091,518 to Sucov. 4 Thus, these undisputed teachings in the prior art, "as filtered through the knowledge of one skilled in the art," *Motorola* , 121 F.3d at 1472, 43 USPQ2d at 1489, as well as the nature of the problem to be solved, provide a suggestion and motivation to use the Stumpo cells, which have heterologous cell surface receptors, in drug screening methods.

SIBIA asserts that, regardless of these express teachings supporting the suggestion to modify Stumpo, various trial testimony provides the substantial evidence on which the jury's implied

finding of no motivation to modify can be supported. SIBIA relies heavily on the testimony of Drs. Wall, Struhl, and Blackshear. Dr. Wall testified that the Stumpo paper contained no mention of drug screening, and that the experiments described in that paper were directed to the characterization of the *fos* gene, not to a drug screening method. Wall also testified that the Stumpo paper would not immediately lead one to "conduct drug screening." Similarly, Dr. Struhl testified that there was no indication that the researchers involved in the experiments described in Stumpo used the cells for drug screening. However, simply pointing out that the Stumpo reference itself does not teach the modification is not substantial evidence of no motivation to modify, given the express teaching of the prior art. SIBIA's reliance on the testimony of Wall and Struhl ignores the possibility that the

motivation to modify Stumpo can be found outside the reference itself. *See id.* Thus, while Stumpo does not expressly suggest that the cells described therein could be used in drug screening methods, the knowledge of those skilled in the art, in particular as embodied in the Lester review article, suggests this modification. SIBIA also points to the testimony of Dr. Blackshear, the senior author of Stumpo, who testified that the Stumpo paper does not contain any reference to drug screening, and at the time those experiments were conducted, "drug screening was not on our minds." However, this testimony, in itself, does not provide substantial evidence in support of the jury's finding. At the time of these experiments, Blackshear was focused on the problem of determining the "fundamental biochemical mechanisms by which insulin worked." Blackshear's personal efforts were limited to a problem different than that addressed by the '629 patent. Thus, the testimony that he was not thinking about drug screening is irrelevant to the fundamental issue of whether the hypothetical person of ordinary skill in the art, when confronted with the problem of developing drug screening methods, would have been motivated to use the Stumpo cells in such methods. *See Pro-Mold & Tool Co.* , 75 F.3d at 1573, 37 USPQ2d at 1630 (discussing the importance of considering the problem to be solved in the obviousness determination); *see also In re Rinehart* , 531 F.2d 1048, 1054, 189 USPQ 143, 149 (CCPA 1976) (same).

Finally, SIBIA points to secondary considerations in support of the jury's verdict. In particular, SIBIA points to three licenses or sub-licenses of the '629 patent, all of which were part of larger

licensing packages. However, the mere existence of these licenses is insufficient to overcome the conclusion of obviousness, as based on the express teachings in the prior art that would have motivated one of ordinary skill to modify Stumpo's cells to be used with unknown compounds. *See Newell Cos. v. Kenney Mfg. Co.* , 864 F.2d 757, 769, 9 USPQ2d 1417, 1426 (Fed. Cir. 1988) (holding that because the record established such a strong case of obviousness based on the teachings of the prior art, the fact that the product was successful does not overcome the conclusion of obviousness). Moreover, SIBIA has failed to point to any evidence establishing a nexus between the licensing activity and the merits of the claimed screening method. *See In re GPAC Inc.* , 57 F.3d 1573, 1580, 35 USPQ2d 1116, 1121 (Fed. Cir. 1995) ("For objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention."). Thus, SIBIA's reliance on secondary considerations in support of the jury verdict must fail.

In sum, the undisputed teaching of the Stumpo paper leads one to within a hairsbreadth of anticipation of claim 1 of the '629 patent. The express teachings in the art provide the motivation and suggestion to modify Stumpo such that the recombinant cells described therein should be used with compounds not previously known to interact with them for purposes of drug screening. SIBIA, the jury verdict winner, has failed to point to any substantial evidence to refute these express teachings, even under the deferential standard with which this court reviews jury verdicts. Thus, claim 1 must be invalidated on the basis of obviousness.

C. Dependent Claims

In addition to finding claim 1 infringed and not invalid, the jury found dependent claims 2, 4-7, 9, 10, 12, and 14 infringed and not invalid as well. However, in this appeal, SIBIA has failed to argue the validity of the dependent claims separately from the validity of claim 1. Thus, these claims do not stand on their own, and given our determination that claim 1 is invalid, the remaining dependent claims must fall as well. *See Mehl/Biophile Int'l Corp. v. Milgraum* , 192 F.3d 1362, 1367, 52 USPQ2d 1303, 1307 (Fed. Cir. 1999); *Gardner v. Tec Sys. Inc.* , 725 F.2d 1338, 1350, 220 USPQ 777, 786 (Fed. Cir. 1984) (en banc) (holding that dependent claims fall with the independent claim on which they depend unless argued separately).

CONCLUSION

We conclude that the implicit finding by the jury that there was no suggestion or motivation to

modify the Stumpo reference is unsupported by substantial evidence and the asserted claims are obvious as a matter of law. Therefore, the district court's denial of the Cadus's motion for JMOL on the issue of invalidity must be

***REVERSED* . COSTS**

Each party shall bear its own costs.

Footnotes

Footnote 1. A cell surface protein is "heterologous" if it is not naturally occurring in the cell.
Footnote 2. Eukaryotic cells, such as animal, plant, yeast, and fungal cells, have nuclei where the cell's genetic material is contained. Prokaryotic cells, such as bacteria and blue-green algae cells, do not have nuclei.
Footnote 3. The "excitability molecules" referred to in Lester are identical to the "cell surface proteins" referred to in the '629 patent.
Footnote 4. Contrary to the suggestion in the dissenting opinion, Sucov is not being "combined" with Stumpo or Lester to achieve the obviousness conclusion. Rather, Sucov is merely cited as an example showing that the use of cells with reporter gene constructs was known in the art to be useful in drug screening methods.

Dissenting Opinion Text

Dissent By:

Mayer, C.J., dissenting.

Today, the court overrides a jury verdict of infringement based on a tenuous obviousness

analysis. It recognizes that the Stumpo paper only refers to the use of known substances and

presumes that, to find infringement, the jury must have implicitly found that there was no motivation in Stumpo to utilize the disclosed cells with compounds not previously known to interact with the cell surface proteins. Based on the state of knowledge in the art that cells with heterologous cell surface proteins were ideal candidates for drug screening methods, the court then concludes that the jury's implicit finding is not supported by substantial evidence.

In reality, the court relies on the combination of Stumpo, Lester, and Sucov to establish that the use of heterologous cells with reporter gene constructs was known in the art to be useful in drug screening methods. Stumpo discloses cells identical to the '629 patent claims, but does not mention their use to test unknown compounds as possible drugs. Lester describes the utility of heterologous cell surface proteins for drug testing, but does not mention cells with reporter gene constructs, which are central to the method of testing of the '629 claims. Sucov was not even argued at trial, where Cadus argued that either Stumpo or Chen renders the '629 patent obvious. This analysis is inconsistent with the court's stated conclusion that the '629 patent is obvious over the Stumpo reference alone in view of the prior art as argued by Cadus. It fails to recognize that the '629 patent includes only method claims; Sibia disclaimed all claims to the cells themselves when Stumpo was brought to its attention.

The court is making an end-run around the requirement that there must be a motivation to modify the reference along the path taken by the '629 patent. *See* *Kolmes v. World Fibers Corp.* , 107 F.3d 1534, 1541, 41 USPQ2d 1829, 1833 (Fed. Cir. 1997) (Invention was not obvious where there was no suggestion or motivation to modify teaching of reference.). It combines a series of references not specifically argued to the jury to conclude that no reasonable jury could possibly find the *absence* of motivation in the prior art to modify the Stumpo paper to render the '629 patent obvious. Without citing any motivation to modify in any of the series of references, the court improperly concludes that it would have been unreasonable for the jury to find as a matter of fact that there was no such motivation. *See* *Tec Air, Inc. v. Denso Mfg. Michigan, Inc.* , 192 F.3d 1353, 1359, 52 USPQ2d 1294, 1297-98 (Fed. Cir. 1999) (Whether a reference provides a motivation to combine its teachings with other references is a question of fact underlying the legal determination of nonobviousness that we assume the jury resolved in favor of the verdict winner and leave undisturbed if it is supported by substantial evidence.).

The district court properly rejected Cadus' motion for judgment as a matter of law, holding that there was substantial evidence to support a verdict of nonobviousness because the '629 patent was a "combination of factors that was not apparent to a person of ordinary skill in the art." The

trial court found additional support for the jury's verdict in evidence of secondary considerations of long-felt need and commercial success of the '629 patent. These are factual underpinnings of the legal conclusion of nonobviousness that the jury presumptively resolved in favor of Sibia because substantial evidence supported them. *See id.* , 52 USPQ2d at 1298.

This court improperly rejects this substantial evidence. It opens the door for accused infringers to string together a series of references, which collectively contain the elements of an apparatus (here, the cell with a heterologous cell surface protein and reporter gene construct) and various suggestions for the use of those separate references. It then would allow an inference of motivation to modify a single reference to render obvious a method claim for utilizing the apparatus. All this is in violation of the well-settled mandate requiring a motivation to alter a single reference or to combine multiple references to render the claims of a patent obvious. *See, e.g.* , *id.* at 1359, 52 USPQ2d at 1298 (motivation to combine multiple references); *B.F. Goodrich v. Aircraft Braking Sys. Corp.* , 72 F.3d 1577, 1582, 37 USPQ2d 1314, 1318 (Fed. Cir. 1996) (motivation to modify a single reference); *Grain Processing Corp. v. American Maize-Products Co.* , 840 F.2d 902, 907, 5 USPQ2d 1788, 1792 (Fed. Cir. 1988) ("Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit.' ") (internal citation omitted); *In re Fine* , 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) ("One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."). The court has substituted itself for the jury, reweighed the evidence, and combined references that were not before the jury. I would sustain the jury's verdict.

- End of Case -

B.F. Goodrich Co. v. Aircraft Braking Systems Corp.

U.S. Court of Appeals Federal Circuit
37 USPQ2d 1314

Decided January 4, 1996
Nos. 95-1112, -1120, -1143

Headnotes

PATENTS

1. Patentability/Validity -- Obviousness -- Relevant prior art -- Particular inventions (§ 115.0903.03)

Patentability/Validity -- Obviousness -- Secondary considerations generally

(§ 115.0907)

Aircraft disk brake assembly employing alternating thick and thin carbon disks is obvious over prior reference describing maintenance schedule for disk brake assembly, since only difference between reference and invention in suit is that asserted claims are limited to initial thick/thin assembly, whereas reference discloses thick/thin arrangement only for replacement of half-worn disks during overhaul, since reference, which teaches maximizing carbon utilization by filling available disk space in brake with any combination of new, partly worn, or reclaimed disks, suggests use of initial thick/thin assembly to one skilled in art, and since secondary considerations are not convincing of nonobviousness in view of minor difference between claimed invention and teachings of reference.

2. Practice and procedure in Patent and Trademark Office -- Prosecution -- Duty of candor -- In general (§ 110.0903.01)

REMEDIES

Monetary -- Attorneys' fees; costs -- Patents -- Exceptional case (§ 510.0905.03)

Federal district court did not clearly err in its findings or abuse its discretion in determining that infringement plaintiff did not engage in inequitable conduct by failing to disclose material prior art references to Patent and Trademark Office during prosecution of patents in suit, since court's

conclusion that evidence of requisite intent to deceive is lacking cannot be held clearly erroneous; plaintiff's conduct in prosecuting patents in suit cannot be condoned, however, since that conduct, including failure to disclose activities that may have implicated on-sale bar of 35 USC 102(b), and submission of careless statements under oath, shows pattern of careless

prosecution that led to grant of patents which are invalid over withheld reference.

Particular patents -- General and mechanical -- Disk brakes

4,742,895, Bok, disk brake assembly, judgment of invalidity affirmed.
4,613,017, Bok, disk brake and method of assembly, judgment of invalidity affirmed.

Case History and Disposition:

Appeal from the U.S. District Court for the District of Delaware, Robinson, J.

Action by The B.F. Goodrich Co. against Aircraft Braking Systems Corp. and Allied- Signal Inc., for patent infringement. From judgment holding patents in suit invalid but finding that plaintiff did not engage in inequitable conduct, parties cross-appeal. Affirmed.

Related decision: 27 USPQ2d 1209

Attorneys:

Harry J. Roper, of Roper & Quigg, Chicago, Ill.; William P. Oberhardt, Raymond N. Nimrod, Ellen D. Law, and Sarah L. Taylor, of Roper & Quigg, Chicago, for B.F. Goodrich Co.

Ray L. Weber, of Renner, Kenner, Greive, Bobak, Taylor & Weber, Akron, Ohio, for Aircraft Braking Systems Corp.

Kenneth W. Starr, of Kirkland & Ellis, Washington, D.C.; Donald G. Kempf Jr., David M. Elston, and Jonathan F. Putnam, of Kirkland & Ellis, Chicago, for Allied-Signal Inc.

Judge:

Before Archer, chief judge, and Newman and Lourie, circuit judges.

Opinion Text

Opinion By:

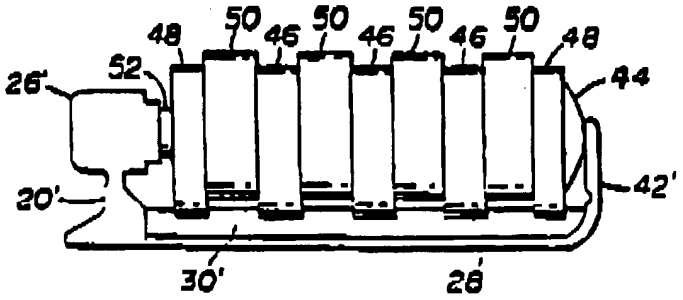
Lourie, J.

The B.F. Goodrich Co. (BFG) appeals from the judgment of the United States District Court for the District of Delaware holding (1) U.S. Patents 4,742,895 and 4,613,017 invalid under 35 U.S.C. Sections 103 and 102(b) and (2) that Aircraft Braking Systems Corp. (ABS) did not infringe either patent. ABS and Allied-Signal Inc. cross- appeal from the district court's judgment that BFG did not engage in inequitable conduct, requesting that the court hold this to be an exceptional case and award them attorney fees under 35 U.S.C. Section 285. *B.F. Goodrich Co. v. Aircraft Braking Sys.* , C.A. Nos. 91- 48/91-515-SLR (D. Del. Nov. 10, 1994). Because we conclude that the patents are invalid under 35 U.S.C. Section 103 and that BFG did not engage in inequitable conduct, we affirm.

BACKGROUND

BFG is the assignee of the '017 and '895 patents. The '017 patent is directed to a method of overhauling a disk brake assembly. The '895 patent is a division of the '017 patent and contains apparatus claims for a disk brake assembly. Both patents are entitled to the benefit of the '017 patent's July 2, 1984 filing date and thus July 2, 1983 is the critical date for purposes of 35 U.S.C. Section 102.

The claimed brake assembly is used in aircraft landing gear wheels. Figure 4 of the patents is a cross-sectional view illustrating the assembly:



The assembly includes stators 46 positioned between rotors 50. The stators 46 and rotors 50 consist of carbon disks and are sandwiched between end plates 48. The rotors 50 are mechanically attached to a rim (not shown) on which is mounted a tire so that, when the wheel rotates, rotors 50 rotate between stators 46. When the brake is activated, piston 26' applies pressure to one of the two end plates 48, which in turn forces together the rotors and stators against end plate 44 so that the resulting friction between the rotors and stators stops the wheel. Eventually, the carbon disks become worn through friction and must be replaced since a minimum thickness of the disks is required to absorb the heat generated by the friction and ensure effective braking operation.

The invention provides a brake assembly having alternating thick and thin disks, referred to as a thick/thin assembly, consisting of, for example, thin stators and thick rotors. The disks tend to wear evenly. Accordingly, when the thin disks become worn to the point of requiring replacement, the thick disks are only half worn. Only the original thin disks are replaced, and they are replaced with thick disks. The process can be repeated, and, during each maintenance interval, only half of the disks are thus replaced.

In comparison, prior art brake assemblies had disks of uniform thickness. During prosecution, the patentee distinguished its invention over this feature of the prior art brake assemblies. In response to a final rejection of

the '017 patent on the ground of obviousness, the applicant submitted an affidavit by Wesley S. Perry, Director of Engineering for BFG. The following are relevant portions of the Perry

affidavit.

That . . . he has not seen or heard of the brake construction and method shown and described in the [BFG patent application];

That as Director of Engineering he had the responsibility for reading the literature and trade journals on aircraft brakes and has attended numerous seminars and trade shows on aircraft brakes;

That at no time in the literature or at seminars and trade shows he has attended, has the brake construction and method shown and described in the [BFG patent application] been suggested;

. . .

That the common practice in overhauling carbon brakes is to replace all the brake disks after they are substantially completely worn with full thickness disks and that it would not be obvious to replace one set of stators or rotors with a new or refurbished set of full thickness disks while the other set is half worn at overhaul intervals shorter than the refurbished interval for the disks as taught and shown in the [BFG patent application];

. . .

That based on his observation and knowledge of the ordinary skilled worker overhauling carbon brakes, the ordinary skilled worker would not have found it expedient through routine experimentation to arrange the rotors and stators of a carbon disk brake with different available wear portions so that after a predetermined number of brake applications said available wear portions of a first group of disks are substantially worn away at an intermediate overhaul time and said available wear portions of a second group of disks are not worn away.

. . .

In response to the submission of this affidavit, the U.S. Patent and Trademark Office (PTO) allowed the application, which issued as the '017 patent. The PTO subsequently allowed the divisional application, which issued as the '895 patent. Claim 1 of the '017 patent and claim 2 of the '895 patent, which are the only independent claims at issue, read as follows:

1. A method of assembling and overhauling a disk brake having a plurality of disks with available wear portions of predetermined different thicknesses comprising positioning a first group of said disks in overlapping relationship with a second group of said disks, said first group of said disks having each of said available wear portions of a first thickness, said second group of said disks having each of said available wear portions of a second thickness, said first thickness of each of said available wear portions of said first group of said disks being less than

said second thickness of each of said available wear portions of said second group of said disks, replacing said first group of said disks with a third group of said disks at an intermediate brake overhaul time when said available wear portions of said first group are substantially fully worn, said available wear portions of each of said third group of said disks having a third thickness greater than the thickness of each of said available wear portions of said second group of said disks at said intermediate brake overhaul time.

2. A disk brake assembly comprising a first group of brake disks and a second group of brake disks in axially aligned and interleaved relationship, said disks of said first group being interleaved with said disks of said second group in alternating relationship, each of said disks of said first group and said second group having oppositely disposed wear surfaces, said wear surfaces on opposite sides of each brake disk of said first group are equal in thickness, said wear surfaces on opposite sides of each brake disk of said second group are equal in thickness, said wear surfaces of said first group of said disks having a first thickness, said wear surfaces of said second group of said disks having a second thickness, said first thickness of said first group of said disks being less than said second thickness of said second group of said disks whereby after a predetermined number of brake applications the available wear thickness of said first group of said disks are substantially fully worn away at an intermediate overhaul time and said available wear thickness of said second group of said disks are not worn away.

During prosecution of the patents, the PTO was apparently not aware of, and hence did not consider, a published paper by employees of Dunlop Ltd. This paper, entitled *The Economic and Safety Aspects of Commercial Aircraft Carbon Brakes* [hereinafter Dunlop], was presented at the International Federation of Airworthiness Annual Conference in Long Beach, California, in April 1982. Although several individuals at BFG had copies of Dunlop in their files, BFG did not cite it to the PTO during prosecution of the patent applications. Relevant portions of Dunlop describe what is referred to as a 2 for 1 refurbishment scheme in which two

worn disks are machined to smoothness and then clipped together to form one "new" disk. Dunlop describes how these thicker 2 for 1 disks can be used with new disks:

Following brake chassis inspection the heat stack can either be put back into the brake for the remainder of its life, or some of the half worn discs can be assembled with re-furbished discs

from other brakes. Because of this arrangement it is possible to use reclaimed discs which are thicker than new discs. In other words, during the machining for reclaim [sic] the minimum amount of carbon has been machined off in order not to waste any of this expensive material. Individually these extra thick discs have a life potential well in excess of 3,000 landings. By the use of this half life inspection routine, and by using extra thick discs mixed with part worn discs the cost per brake landing can be reduced significantly.

Id. at 11. Dunlop also teaches obtaining maximum use of the carbon disks by building up the heat stack to fill the space available for the disks by using a combination of new and refurbished disks. *Id.* at 12.

In addition, Dunlop describes brake overhaul schedules using the 2 for 1 refurbishment technique. A chart in Dunlop illustrates the overhaul schedules. Aircraft are listed on the left side of the chart, and the months from October 1984 through June.1988 are listed across the top of the chart. The chart contains boxes representing a particular overhaul for the corresponding aircraft and month. The chart also contains a description of several overhaul routines, the most relevant of which are referred to as overhaul combinations 3 and 5. The description for combination 3 states: "New stators, pressure and thrust stators, half worn rotors." That for combination 5 states: "New rotors, half worn stators, pressure and thrust stators." Combinations 3 and 5, therefore, together describe an overhaul scheme involving a thick/thin aircraft brake assembly.

BFG also failed to submit to the PTO other prior art that it was aware of during its prosecution of the patents. This prior art included a Concorde manual, which describes a brake overhaul method used on the Concorde, which was the first commercial aircraft to use carbon disk brakes. According to this method, new or partially worn disks were placed in the brake assembly during overhaul. Thus, after use in this manner, the carbon disks in the Concorde brake had varying thicknesses.

Other prior art also included U.S. Patent 3,480,115, which describes a brake assembly having steel disks arranged in descending order of thickness. BFG had itself used brake assemblies with steel rotors of different wear thicknesses.

BFG also failed to notify the PTO of certain of its own activities which may have implicated the on-sale bar under 35 U.S.C. Section 102(b). BFG made a presentation in France to Airbus Industries, which has customers in the United States, concerning the brake assembly in January 1983. Later, BFG met with representatives of Boeing on March 24, 1983 in Seattle, Washington,

in order to discuss BFG's carbon brakes. This meeting was part of an ongoing effort by BFG to interest Boeing in its thick/thin carbon aircraft brake assemblies. Even though these activities occurred before the critical date, BFG failed to disclose them to the PTO during prosecution of the '017 and '895 patents. Moreover, the inventor, Lowell D. Bok, stated in his invention record, which he submitted to a BFG in-house attorney, that the BFG thick/thin brake assemblies had been "proposed for the 757-200, A310-300 and 767-300 Aircraft [.]"

BFG sued ABS and Allied-Signal separately for infringement of claims 2 and 3 of the '895 patent and claims 1-4 of the '017 patent. Both defendants counterclaimed for a declaratory judgment of invalidity and unenforceability, and the cases were consolidated for discovery and a bench trial. In its memorandum opinion following the trial, the district court held that: (1) claims 2 and 3 of the '895 patent and claims 1-4 of the '017 patent were invalid under 35 U.S.C. Section 103 as having been obvious over Dunlop and under 35 U.S.C. Section 102(b) as having been on sale by virtue of BFG's activities before the critical date; (2) Allied-Signal infringed claims 2 and 3 of the '895 patent and claims 1-4 of the '017 patent; (3) ABS did not infringe any of the asserted claims; and (4) BFG did not engage in inequitable conduct during prosecution of the patents. On appeal, BFG challenges the district court's decision on validity and on infringement by ABS. On cross- appeal, ABS and Allied-Signal challenge the district court's holding that BFG did not engage in inequitable conduct.

DISCUSSION

A. *Obviousness*

We review the district court's conclusion of obviousness *de novo* as a matter of law. *See Jervis B. Webb Co. v. Southern Sys., Inc.* , 742 F.2d 1388, 1393, 222 USPQ 943, 946 (Fed. Cir. 1984). A determination of obviousness is based on factual inquiries, *Graham v. John Deere Co.* , 383 U.S. 1,

17-18, 148 USPQ 459, 467 (1966), which we review under the clearly erroneous standard. Fed. R. Civ. P. 52(a); *Webb* , 742 F.2d at 1393, 222 USPQ at 946; *see also Uniroyal, Inc. v. Rudkin-Wiley Corp.* , 837 F.2d 1044, 1050, 5 USPQ2d 1434, 1438 (Fed. Cir.) ("The factual findings of the district court underlying the obviousness determination will be overturned on

appeal only if they are clearly erroneous."), *cert. denied* , 488 U.S. 825 (1988).

BFG argues that the district court erred in holding the inventions of the '895 and '017 patents to have been obvious over Dunlop. BFG contends that there was no suggestion or motivation to modify the teachings of Dunlop to obtain the claimed invention. In addition, BFG alleges that the district court misconstrued or failed to credit evidence of secondary considerations such as commercial success, copying by others, satisfying a long-felt need, and providing significant unexpected advantages.

ABS and Allied-Signal counter that the district court did not err in finding the invention to have been obvious over Dunlop. They contend that Dunlop suggested the claimed invention to one skilled in the art. They further argue that the evidence of secondary considerations presented by BFG only served to reinforce the conclusion of obviousness.

Obviousness under 35 U.S.C. Section 103 is a legal conclusion involving four factual inquiries. *Uniroyal* , 837 F.2d at 1050, 5 USPQ2d at 1438. These inquiries consist of: "(1) the scope and content of the prior art; (2) the differences between the claims and the prior art; (3) the level of ordinary skill in the pertinent art; and (4) secondary considerations, if any, of nonobviousness." *Id.* Secondary considerations include evidence of factors tending to show nonobviousness, such as commercial success of the invention, satisfying a long-felt need, failure of others to find a solution to the problem at hand, and copying of the invention by others. *Id.* ; *Panduit Corp. v. Dennison Mfg. Co.* , 810 F.2d 1561, 1566, 1 USPQ2d 1593, 1595 (Fed. Cir.), *cert. denied* , 481 U.S. 1052 (1987).

When obviousness is based on a particular prior art reference, there must be a showing of a suggestion or motivation to modify the teachings of that reference. *E.g.* , *ACS Hosp. Sys., Inc. v. Montefiore Hosp.* , 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). This suggestion or motivation need not be expressly stated. *Cable Elec. Prods., Inc. v. Genmark, Inc.* , 770 F.2d 1015, 1025, 226 USPQ 881, 886 (Fed. Cir. 1985).

The district court found that the invention was obvious over Dunlop. The level of ordinary skill in the art was not in dispute, nor was the scope of the prior art, which included the Dunlop paper, the steel brake art such as was described in U.S. Patent 3,480,115, and the Concorde manual. The difference between Dunlop and the claimed inventions is relatively minor. The district court found that the only real difference is that the claims are limited to an *initial* thick/thin assembly whereas Dunlop discloses the thick/thin arrangement only for replacement of half-worn disks during brake overhaul. The district court stated that "Figure 14 [the overhaul

schedule] plainly contemplates the continuation of the series of overhauls beyond the last date covered in the chart." The district court held that the overhaul schedule in Dunlop itself provided the suggestion for an initial thick/thin carbon brake assembly and hence rendered the claimed invention obvious.

The district court also analyzed the secondary considerations presented by BFG. It did not find that they overcame the strong teachings of the prior art. The assertion of "long-felt need" was discounted because the BFG invention was similar to the teachings of Dunlop. The failure of others was not found to be significant because there was only a brief time period during which manufacturers sought a solution to the problem of increased carbon utilization in aircraft brakes. Only slight evidence of skepticism by others was presented. Copying by others was not found to be compelling because there was no extensive development by competitors, and a noninfringing substitute was easily designed. The advantages of the invention were not found to be necessarily unexpected given the state of the prior art. Finally, the district court found that the evidence of commercial success was ambiguous.

We conclude that the district court's factual findings regarding the four *Graham* inquiries were not clearly erroneous. *See* Fed. R. Civ. P. 52(a) (1995). As explained above, these findings were supported by the evidence of record, and we do not have a definite and firm conviction that a mistake was made as to those findings. *See United States v. United States Gypsum Co.* , 333 U.S. 364, 395 [76 USPQ 430] (1948) ("A finding is 'clearly erroneous' when although there is evidence to support it, the reviewing court on the entire evidence is left with the definite and firm conviction that a mistake has been committed.").

[1] In addition, we agree with the district court's ultimate conclusion of obviousness. As the district court recognized, the overhaul schedule in Dunlop contemplates continuation of the combination 3 and 5 overhaul methods. Dunlop also teaches maximizing

carbon utilization by filling the "envelope," the space available for disks in the brake, using any combination of new or part worn or reclaimed disks. In addition, ABS's and Allied- Signal's expert witness, as well as BFG's expert witness, testified that those skilled in the art would know to fill the brake "envelope" to obtain maximum use of the available space. BFG has indicated a connection between an initial thick/thin assembly and "filling the envelope."

Moreover, as the inventor himself agreed, if a thick/thin arrangement makes sense for an overhaul, it would seem to be logical to adopt it *ab initio* . Accordingly, the teachings of Dunlop, to one skilled in the art, provide a suggestion of an initial thick/thin brake assembly. We also agree with the district court that the secondary considerations were not convincing of nonobviousness. Considering the minor difference between the claimed invention and the teachings of Dunlop, the secondary considerations were not sufficiently compelling. *See Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.* , 776 F.2d 281, 291-92, 227 USPQ 657, 663 (Fed. Cir. 1985).

Because we hold that claims 2 and 3 of the '895 patent and claims 1-4 of the '017 patent are invalid as having been obvious over Dunlop, we need not reach the issues relating to the on-sale bar and infringement.

B. *Inequitable Conduct*

A determination of inequitable conduct is committed to the district court's discretion. Accordingly, we review the district court's judgment under the abuse of discretion standard. *Kingsdown Medical Consultants, Ltd. v. Hollister, Inc.* , 863 F.2d 867, 876, 9 USPQ2d 1384, 1392 (Fed. Cir. 1988), *cert. denied* , 490 U.S. 1067 (1989). To overturn such a discretionary ruling of a district court, "the appellant must establish that the ruling is based on clearly erroneous findings of fact or on a misapplication or misinterpretation of applicable law, or evidences a clear error of judgment on the part of the district court." *Molins PLC v. Textron, Inc.* , 48 F.3d 1172, 1178, 33 USPQ2d 1823, 1827 (Fed. Cir. 1995).

ABS and Allied-Signal allege inequitable conduct with respect to several pieces of prior art. In particular, they allege that BFG engaged in inequitable conduct in its failure to disclose to the PTO Dunlop, the Concorde manual, U.S. Patent 3,480,115 showing an example of the steel brake art, BFG's own steel brake prior art, and BFG's activities with Boeing and Airbus. They also allege that the statements in the Perry affidavit provide evidence of an intent to mislead.

BFG argues that there was no intent by the inventor, Bok, or his attorneys to mislead the PTO. BFG asserts that there is no evidence that Bok or his attorneys knew of Dunlop during prosecution. While they of course knew of the Boeing and Airbus activities, BFG argues that it had a reasonable belief that these activities did not violate the on-sale bar. BFG also argues that the Perry affidavit does not show an intent to mislead the PTO, because all the statements in the affidavit were true.

Inequitable conduct consists of an "affirmative misrepresentation of a material fact, failure to

disclose material information, or submission of false material information, coupled with an intent to deceive." *Molins* , 48 F.3d at 1178, 33 USPQ2d at 1826. One alleging inequitable conduct must prove the threshold elements of materiality and intent by clear and convincing evidence. *Id.* , 33 USPQ2d at 1826-27. The district court must then weigh the threshold findings of materiality and intent in light of all the circumstances to determine whether the equities warrant a conclusion that inequitable conduct occurred. *Id.*

Much of the prior art involved here certainly was material. Dunlop was directly relevant to the problem addressed by the '017 and '895 patents; it discloses techniques for increased carbon utilization in aircraft brakes, as well as a thick/thin aircraft brake assembly. BFG's sales activities were also material, because they were potential statutory bars under 35 U.S.C. Section 102(b). The steel brake art included brakes having steel disks of varying thickness, and the Concorde manual disclosed carbon brakes with disks of varying thickness. All of this prior art was thus arguably material.

The focus of the inequitable conduct issue in this case must thus be on intent, which is a question of fact. *See Molins* , 48 F.3d at 1178, 33 USPQ2d at 1827. We must affirm the district court on this issue unless its finding was clearly erroneous. *Id.* The district court was troubled by BFG's conduct, but essentially gave it the benefit of the doubt because determinations of obviousness and the applicability of the on-sale bar are often close and subject to varying reasonable interpretations. In particular, the district court stated that " [t]he application of the on-sale bar in Section 102(b) and the factors determining obviousness under Section 103 is by no means a certain enterprise, and the fact that the Court has found the patents invalid on these grounds does not mean that BFG's failure to submit this art and information in connection with its patent applications was intentionally misleading."

[2] We too are troubled by BFG's conduct, but conclude that the district court did not clearly err in its findings or abuse its discretion in determining that BFG did not engage in inequitable conduct. " [A] finding that particular conduct amounts to 'gross negligence' does not of itself justify an inference of intent to deceive; the involved conduct, viewed in light of all the evidence, including evidence indicative of good faith, must indicate sufficient culpability to

require a finding of intent to deceive." *Kingsdown* , 863 F.2d at 876, 9 USPQ2d at 1392.
There was a basis for the patent attorney prosecuting the applications to conclude that BFG's meeting with Boeing did not trigger the on-sale bar on the ground that it was a technical, not a sales, meeting, and thus that it need not have been disclosed to the PTO. Prudence would have dictated otherwise, but the requisite evidence of intent to deceive is lacking. In addition, the Airbus activity seemingly occurred outside the United States, and its nondisclosure does not reveal an intent to deceive. Even though Dunlop was in the files of several BFG employees, it is not clear that Bok and his attorney possessed it. The evidence tends to show that Bok only became aware of Dunlop after the '017 and '895 patents issued, and the patent attorney was not on the circulation list to receive the publication. There is also a letter of record from BFG to a foreign attorney indicating after the patents issued that BFG had just recently become aware of Dunlop. The other alleged prior art is similarly not associated with evidence of an intent to deceive.
The Perry affidavit is more troubling, but also falls short of providing an inference of an intent to mislead the PTO. While the statements in the affidavit are true, as BFG asserts, this alone does not negate a finding of inequitable conduct, since truthful statements can be crafted in a misleading manner through intentional omission of particular relevant facts. However, there is no evidence of intentional omission of relevant facts in the affidavit and, in particular, no evidence that Perry in fact knew of Dunlop. While Perry was not called as a witness at trial due to an agreement between the parties, relevant portions of his deposition transcript are of record. In Perry's deposition, he testified that he "may have seen it [Dunlop] before," but did not "specifically remember seeing it." He also testified that he did not recall seeing the copy of Dunlop on which his name was handwritten as part of a circulation list. The district court's conclusion that evidence of intent to deceive is lacking cannot be said to be clearly erroneous.
We have considered whether the totality of the actions here lead to an inference of an intent to deceive even though the individual instances do not. We arrive at the same conclusion, lack of evidence of intent. It is not surprising that those who are careless exhibit those qualities more than once. It still does not demonstrate, without more, an intent to deceive. Accordingly, we conclude that the district court did not clearly err in its finding of lack of intent to deceive or abuse its discretion in finding that BFG did not engage in inequitable conduct. In the absence of an intent to deceive, courts cannot find inequitable conduct merely because patents are held invalid over the relevant prior art. Having affirmed the district court's conclusion that there was

no inequitable conduct, we also affirm its conclusion that this case was not exceptional and hence its denial of attorney fees.

Our conclusion does not mean, however, that we condone BFG's conduct in prosecuting the '017 and '895 patents. Barely dodging a bullet based on our deference to a trial court's decision on the factual question of intent and on a matter of equity does not merit approval or justify complacency. BFG's conduct shows a pattern of careless patent prosecution. It has led to the grant of a patent which is invalid over a withheld reference. While we have not reviewed the holding of invalidity based upon the on-sale bar, there certainly was a close question concerning that uncited event. The Perry affidavit evidences questionable conduct, considering that Perry's name was on a circulation list for Dunlop and that he stated in his affidavit that he was responsible for knowing the literature on aircraft brakes and that he had never seen a brake assembly as described and shown in the '017 and '895 patents. Submission of careless statements under oath deserves criticism, but, as noted above, we are not able to conclude that the district court erred in failing to find intent to deceive from these actions.

CONCLUSION

Because the district court did not err in holding the '017 and '895 patents invalid on the ground of obviousness, we affirm the district court's judgment of invalidity. Because the district court did not err in holding that BFG did not engage in inequitable conduct due to insufficient evidence of an intent to deceive the PTO in prosecuting the '017 and '895 patents, we affirm the district court's judgment regarding inequitable conduct, and we deny ABS's and Allied-Signal's request for attorney fees. In light of our

holding that the '017 and '895 patents are invalid on the ground of obviousness, the issues relating to the on-sale bar and infringement are moot. *AFFIRMED* .

- End of Case -

In re Bell

U.S. Court of Appeals Federal Circuit
26 USPQ2d 1529

Decided April 20, 1993
No. 92-1375

Headnotes

PATENTS

1. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Patentability/Validity -- Obviousness -- Relevant prior art -- Particular inventions (§ 115.0903.03)

Established relationship in genetic code between nucleic acid and protein it encodes does not make gene prima facie obvious over its correspondent protein in same way that closely related homologs, analogs, and isomers in chemistry may create prima facie case, since there are vast number of nucleotide sequences that might code for specific protein due to "degeneracy" of genetic code; gene might be obvious over correspondent protein if latter is known amino acid sequence specified exclusively by "unique" codons, but claims in application for nucleic acid molecules containing human sequences coding for human insulin-like growth factors I and II (IGF) are not obvious in view of cited prior art disclosing amino acid sequences for IGF I and II, since cited art suggests nearly infinite number of sequences, but fails to suggest which of those are human nucleic acid sequences coding for IGF.

2. Patentability/Validity -- Obviousness -- Combining references (§ 115.0905)

Reference disclosing general method for isolating genes, in combination with prior art disclosing amino acid sequences for insulin-like growth factors I and II (IGF), does not render obvious application claims for nucleic acid molecules containing human sequences coding for human IGF I and II, since, absent some teaching or suggestion supporting combination, obviousness is not established by combining teachings of prior art to produce claimed invention, since reference in question teaches away from invention claimed in application by emphasizing importance of "unique" codons, and since reference thus cannot be held to "fairly suggest" that its teachings be combined with those of prior art, which discloses amino acid sequences lacking "unique" codons.

3. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Patent construction -- Claims -- Process (§ 125.1309)

Similarities between method by which applicants made claimed nucleic acid molecules, and method for isolating genes taught by prior art reference, do not render application claims obvious, since applicants claim compositions, rather than method of making them.

Case History and Disposition:

Appeal from the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences.

Patent application of Graeme I. Bell, Leslie B. Rall and James P. Merryweather, serial no. 07/065,673 ("preproinsulin-like growth factors I and II"). From decision affirming examiner's final rejection of claims 25-46, applicants appeal. Reversed.

Attorneys:

Robert P. Blackburn, Emeryville, Calif. (Debra A. Shetka and Thomas E. Ciotti, of Morrison & Foerster, Palo Alto, Calif., and Donald S. Chisum, of Morrison & Foerster, Seattle, Wash., on brief), for appellant.

Teddy S. Gron, associate solicitor (Fred E. McKelvey, solicitor, on brief; John W. Dew hirst, Lee E. Barrett, Richard E. Schafer, and Albin F. Drost, of counsel), for PTO.

Judge:

Before Rich, Lourie, and Schall, circuit judges.

Opinion Text

Opinion By:
Lourie, J.

Applicants Graeme I. Bell, Leslie B. Rall, and James P. Merryweather (Bell) appeal from the March 10, 1992 decision of the U.S. Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences, Appeal No. 91-1124, affirming the examiner's final rejection of claims 25-46 of application Serial No. 065,673, entitled "Preproinsulin-Like Growth Factors I and II," as unpatentable on the ground of obviousness under 35 U.S.C. Section 103 (1988). Because the Board erred in concluding that the claimed nucleic acid molecules would have been obvious in light of the cited prior art, we reverse.

BACKGROUND

The claims of the application at issue are directed to nucleic acid molecules (DNA and

RNA)1 containing human sequences 2 which code for human insulin-like growth factors I and II (IGF), single chain serum proteins that play a role in the mediation of somatic cell growth following the administration of growth hormones.3
The relevant prior art consists of two publications by Rinderknecht 4 disclosing amino acid sequences for IGF-I and -II and U.S. Patent 4,394,443 to Weissman et al., entitled "Method for Cloning Genes." Weissman describes a general method for isolating a gene for which at least a short amino acid sequence of the encoded protein is known. The method involves preparing a nucleotide probe corresponding to the known amino acid sequence and using that probe to isolate the gene of interest. It teaches that it is advantageous to design a probe based on amino acids specified by unique codons. 5 The Weissman patent specifically describes the isolation of a gene which codes for human histocompatibility antigen, a protein unrelated to IGF. It describes

the design of the probe employed, stating that it was based on amino acids specified by unique codons.

The examiner rejected the claims as obvious over the combined teachings of Rinderknecht and Weissman. She determined that it would have been obvious, "albeit tedious," from the teachings of Weissman to prepare probes based on the Rinderknecht amino acid sequences to obtain the claimed nucleic acid molecules. According to the examiner, "it is clear from [Weissman] that the ordinary artisan knows how to find the nucleic acid when the amino acid sequence is known" and that "the claimed sequences and hosts would have been readily determinable by and obvious to those of ordinary skill in the art at the time the invention was made."

The Board affirmed the examiner's rejection, holding that the examiner had established a *prima facie* case of obviousness for the claimed sequences "despite the lack of conventional indicia of obviousness, e.g., structural similarity between the DNA which codes for IGF-I and the amino acid sequence of the polypeptide which constitues [sic] IGF-I." Slip op. at 6. The Board reasoned that "although a protein and its DNA are not structurally similar, they are correspondently linked via the genetic code." *Id*. at 4 n.1. In view of Weissman, the Board concluded that there was no evidence "that one skilled in the art, knowing the amino acid sequences of the desired proteins, would not have been able to predictably clone the desired

DNA sequences without undue experimentation." *Id.* at 8.

The issue before us is whether the Board correctly determined that the amino acid sequence of a protein in conjunction with a reference indicating a general method of cloning renders the gene *prima facie* obvious.

DISCUSSION

We review an obviousness determination by the Board *de novo*. *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Bell argues that the PTO has not shown how the prior art references, either alone or in combination, teach or suggest the claimed invention, and thus that it has failed to establish a *prima facie* case of obviousness.

We agree. The PTO bears the burden of establishing a case of *prima facie* obviousness. *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). "A prima facie case of

obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art." *In re Rinehart*, 531 F.2d 1048, 1051, 189 USPQ 143, 147 (CCPA 1976).

The Board supported the examiner's view that the "correspondent link" between a gene and its encoded protein via the genetic code renders the gene obvious when the amino acid sequence is known. In effect, this amounts to a rejection based on the Rinderknecht references alone. Implicit in that conclusion is the proposition that, just as closely related homologs, analogs, and isomers in chemistry may create a *prima facie* case, *see In re Dillon*, 919 F.2d 688, 696, 16 USPQ2d 1897, 1904 (Fed. Cir. 1990) (*in banc*), *cert. denied* , 111 S. Ct. 1682 (1991), the established relationship in the genetic code between a nucleic acid and the protein it encodes also makes a gene *prima facie* obvious over its correspondent protein.

[1] We do not accept this proposition. It may be true that, knowing the structure of the protein, one can use the genetic code to hypothesize possible structures for the corresponding gene and that one thus has the potential for obtaining that gene. However, because of the degeneracy of the genetic code, there are a vast number of nucleotide sequences that might code for a specific protein. In the case of IGF, Bell has argued without contradiction that the Rinderknecht amino acid sequences could be coded for by more than 10^{36} different nucleotide sequences, only a few of which are the human sequences that Bell now claims. Therefore, given the nearly infinite number of possibilities suggested by the prior art, and the failure of the cited prior art to suggest which of those possibilities is the human sequence, the claimed sequences would not have been obvious.

Bell does not claim all of the 10^{36} nucleic acids that might potentially code for IGF. Neither does Bell claim all nucleic acids coding for a protein having the biological activity of IGF. Rather, Bell claims only the human nucleic acid sequences coding for IGF. Absent anything in the cited prior art suggesting which of the 10^{36} possible sequences suggested by Rinderknecht corresponds to the IGF gene, the PTO has not met its burden of establishing that the prior art would have suggested the claimed sequences.

This is not to say that a gene is never rendered obvious when the amino acid sequence of its coded protein is known. Bell concedes that in a case in which a known amino acid sequence is specified exclusively by unique codons, the gene might have been obvious. Such a case is not before us. 6 Here, where Rinderknecht suggests a vast number of possible nucleic acid

sequences, we conclude that the claimed human sequences would not have been obvious.
[2] Combining Rinderknecht with Weissman does not fill the gap. Obviousness " 'cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination.' " *In re Fine,* 837 F.2d at 1075, 5 USPQ2d at 1598 (citing *ACS Hosp. Sys. v. Montefiore Hosp.,* 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)). What a reference teaches and whether it teaches toward or away from the claimed invention are questions of fact. *See Raytheon Co. v. Roper Corp.,* 724 F.2d 951, 960-61, 220 USPQ 592, 599-600 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 [225 USPQ 232] (1984).
While Weissman discloses a general method for isolating genes, he appears to teach away from the claimed invention by emphasizing the importance of unique codons for the amino acids. Weissman suggests that it is generally advantageous to design a probe based on an amino acid sequence specified by unique codons, and also teaches that it is "counterproductive" to use a primer having

more than 14-16 nucleotides unless the known amino acid sequence has 4-5 amino acids coded for by unique codons. Bell, in contrast, used a probe having 23 nucleotides based on a sequence of eight amino acids, none of which were unique. Weissman therefore tends to teach away from the claimed sequences since Rinderknecht shows that IGF-I has only a single amino acid with a unique codon and IGF-II has none.
The PTO, in urging us to affirm the Board, points to the suggestion in Weissman that the disclosed method can "easily" be applied to isolate genes for an array of proteins including peptide hormones. The PTO thus argues that in view of Weissman, a gene is rendered obvious once the amino acid sequence of its translated protein is known. We decline to afford that broad a scope to the teachings of Weissman. While "a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests," *In re Burckel,* 592 F.2d 1175, 1179, 201 USPQ 67, 70 (CCPA 1979), we cannot say that Weissman "fairly suggests" that its teachings should be combined with those of Rinderknecht, since it nowhere suggests how to apply its teachings to amino acid sequences without unique codons.
We conclude that the Board clearly erred in determining that Weissman teaches toward, rather

than away from, the claimed sequences. Therefore, the requisite teaching or suggestion to combine the teachings of the cited prior art references is absent, *see In re Fine*, 837 F.2d 1075, 5 USPQ2d at 1599, and the PTO has not established that the claimed sequences would have been obvious over the combination of Rinderknecht and Weissman.

[3] Finally, the PTO emphasizes the similarities between the method by which Bell made the claimed sequences and the method taught by Weissman. The PTO's focus on Bell's method is misplaced. Bell does not claim a method. Bell claims compositions, and the issue is the obviousness of the claimed compositions, not of the method by which they are made. *See In re Thorpe,* 777 F.2d 695, 697, 227 USPQ 964, 966 (Fed. Cir. 1985) ("The patentability of a product does not depend on its method of production.").

CONCLUSION

Because we conclude that the combination of prior art references does not render the claimed invention obvious, we reverse the Board's decision affirming the examiner's rejection of claims 25-46.

REVERSED

Footnotes

Footnote 1. A basic familiarity with recombinant DNA technology is presumed. For a general discussion, *see In re O'Farrell*, 853 F.2d 894, 895-99, 7 USPQ2d 1673, 1674-77 (Fed. Cir. 1988).

Footnote 2. Interchangeably referred to as "native" sequences and "genes."

Footnote 3. Claim 25 is conceded to be representative of the claims at issue:

A composition comprising nucleic acid molecules containing a human sequence encoding insulin-like growth factor (hIGF) substantially free of nucleic acid molecules not containing said hIGF sequence, wherein said hIGF sequence is selected from the group consisting of:

(a) 5 '-GGA CCG GAG ACG CUC UGC GGG GCU GAG CUG GUG GAU GCU CUU CAG

UUC GUG UGU GGA GAC AGG GGC UUU UAU UUC AAC AAG CCC ACA GGG UAU GGC UCC AGC AGU CGG AGG GCG CCU CAG ACA GGU AUC GUG GAU GAG UGC UGC UUC CGG AGC UGU GAU CUA AGG AGG CUG GAG AUG UAU UGC GCA CCC CUC AAG CCU GCC AAG UCA GCU-3 ', wherein U can also be T;

(b) 5 '-GCU UAC CGC CCC AGU GAG ACC CUG UGC GGC GGG GAG CUG GUG GAC ACC CUC CAG UUC GUC UGU GGG GAC CGC GGC UUC UAC UUC AGC AGG CCC GCA AGC CGU GUG AGC CGU CGC AGC CGU GGC AUC GUU GAG GAG UGC UGU UUC CGC AGC UGU GAC CUG GCC CUC CUG GAG ACG UAC UGU GCU ACC CCC GCC AAG UCC GAG-3 ', wherein U can also be T;

(c) nucleic acid sequences complementary to (a) or (b); and

(d) fragments of (a), (b) or (c) that are at least 18 bases in length and which will selectively hybridize to human genomic DNA encoding hIGF.

The other rejected claims are apparently directed to cellular hosts transformed with the claimed nucleic acid sequences. Because their fate is dependent upon that of claim 25, neither appellant nor the Patent and Trademark Office have considered them separately and we will not do so either.

Footnote 4. Rinderknecht et al., *The Amino Acid Sequence of Human Insulin-like Growth Factor I and Its Structural Homology with Proinsulin* , 253 The Journal of Biological Chemistry 2769-76 (1978); Rinderknecht et al., *Primary Structure of Human Insulin-like Growth Factor II* , 89 FEB Letters 283-86 (May 1978).

Footnote 5. A sequence of three nucleotides, called a codon, codes for each of the twenty natural amino acids. Since there are twenty amino acids and sixty-four possible codons, most amino acids are specified by more than one codon. This is referred to as "degeneracy" in the genetic code. The term "unique" refers to an amino acid coded for by a single codon. *See Amgen Inc. v. Chugai Pharmaceutical Co.* , 927 F.2d 1200, 1207-08 n.4, 18 USPQ2d 1016, 1022 n.4 (Fed. Cir.), *cert. denied* , 112 S. Ct. 169 (1991).

Footnote 6. We also express no opinion concerning the reverse proposition, that knowledge of the structure of a DNA, e.g., a cDNA, might make a coded protein obvious.

- End of Case -

In re Gorman

U.S. Court of Appeals Federal Circuit
18 USPQ2d 1885

Decided May 13, 1991
No. 90-1362

Headnotes

PATENTS

1. Patentability/Validity - Obviousness - Combining references (§ 115.0905)

Patent and Trademark Office's reliance on teachings of large number of references in rejecting patent application for obviousness does not, without more, weigh against holding of obviousness on appeal, since criterion is not number of references, but whether references are in fields which are same as or analogous to field of invention, and whether their teachings would, taken as whole, have made invention obvious to person skilled in that field.

2. Patentability/Validity - Construction of claims (§ 115.03)

Patentability/Validity - Obviousness - In general (§ 115.0901)

Claim which describes features of invention in great detail is nevertheless obvious in view of prior art, since claim that is narrowly and specifically drawn must still meet requirements of 35 USC 103, and details listed in claim are shown in references and thus do not contribute to unobviousness.

3. Patentability/Validity - Obviousness - Relevant prior art - Particular inventions (§ 115.0903.03)

Patentability/Validity - Obviousness - Combining references (§ 115.0905)

Application claim for candy sucker on stick, molded in elastomeric mold in shape of human thumb, is obvious in view of prior art, since all elements of claim, including molded lollipop having chewing gum base plug, with elastomeric mold serving as product wrapper, and candy in shape of human thumb, are shown in prior art references in various subcombinations, used in same manner and for same purpose as in claimed invention.

Case History and Disposition:

Appeal from the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences.

Patent application of Jeffrey B. Gorman and Marilyn Katz, serial no. 06/882,480 (composite food product). From decision of Board of Patent Appeals and Interferences upholding examiner's rejection of all claims in application, applicants appeal. Affirmed.

Attorneys:

Thomas W. Tolpin, Highland Park, Ill., for appellant.

Teddy S. Gron, associate solicitor (Fred E. McKelvey, solicitor, with him on brief), for appellee.

Judge:

Before Rich, Newman, and Rader, circuit judges.

Opinion Text

Opinion By:

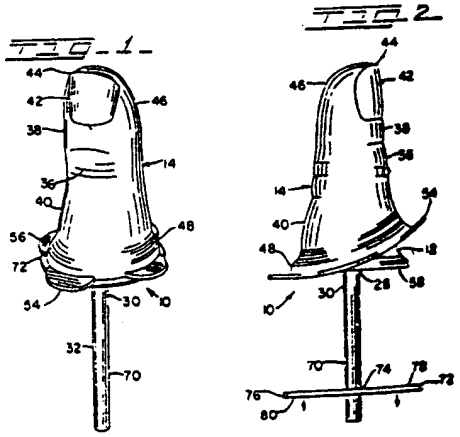
Newman, J.

Jeffrey B. Gorman and Marilyn Katz (hereinafter "Gorman") appeal the decision of the United States Patent and Trademark Office, Board of Patent Appeals and Interferences (the "Board") denying patentability to all the claims of Gorman's patent application Serial No. 06/882,480, entitled "Composite Food Product." We affirm.

The Invention

The claimed invention is a composite candy sucker on a stick, molded in an elastomeric mold in the shape of a human thumb. During the manufacturing process liquid candy is poured into the mold, and an edible plug of bubble or chewing gum or chocolate or food-grade wax is poured into the mold after the candy has hardened, serving as a seal for the end portion of the candy. A paper or plastic disc abuts and covers the plug. The mold serves as a cover that can be removed from the candy by means of protruding flanges. The cover is described as a "toy and novelty item".

Figure 1 shows the invention in the form in which it is marketed. Figure 2 shows the cover partially removed to reveal the candy portion (12) and the chewable or edible plug (58):



The claims describe the product in detail, as is apparent from claim 16, the claim pressed by Gorman in this appeal:

16. A composite food product, comprising:

a candy core, said candy core being in a generally liquified form when formulated,

heated, blended and poured into a mold and in a substantially thumb-shaped hardened form when cooled and removed from said mold;

said thumb-shaped hardened form comprising said candy core positioned along a vertical axis

and comprising a rigid joint-shaped portion, a rigid upper portion extending upwardly from said rigid joint-shaped portion along said vertical axis, and a rigid lower portion extending downwardly from said rigid joint-shaped portion along said vertical axis, said upper portion having a rigid finger nail-shaped portion with an upper rigid tip providing a rigid top end of said thumb-shaped hardened form and a rigid convex back extending rearwardly and downwardly from said rigid tip, and said rigid lower portion having a rigid bottom end and defining a recessed opening comprising a handle-receiving socket about said vertical axis;
a removable resilient shell comprising a substantially thumb-shaped, elastomeric material selected from the group consisting of rubber and flexible plastic, said shell providing a mold for receiving and molding said liquified candy form,
a removable outer protective cover positioned about and covering said hardened form comprising said candy core, and
a toy and novelty item for placement upon the thumb of the user when removed from said hardened form comprising said candy core;
said thumb-shaped elastomeric material comprising said removable resilient shell comprising a flexible joint-shaped portion, a flexible upper portion extending upwardly from said flexible joint-shaped portion along said vertical axis, and a flexible lower portion extending downwardly from said flexible joint-shaped portion along said vertical axis, said upper portion having a flexible finger nail-shaped portion with an upper flexible tip providing a flexible top end of said shell and a flexible convex back extending rearwardly and downwardly from said flexible tip, and said flexible lower portion having an enlarged open ended diverging base, said base having a larger circumference and transverse cross-sectional area than other portions of said shell and providing the bottom of said shell, said open ended base defining a plug-receiving chamber and an access opening for entrance of said liquified form and discharge of said hardened candy form, and a set of substantially symmetrical arcuate lobes extending radially outwardly from said base, said lobes being circumferentially spaced from each other and providing manually grippable flange portions to facilitate manual removal of said shell from said core;
a plug positioned in said plug-receiving chamber adjacent said bottom of said shell, said plug abutting against the bottom of said core and providing a cap for substantially plugging and sealing the open end of said mold and cover to help enclose said candy core, and said plug comprising a food grade material selected from the group consisting of bubble gum, chewing gum, chocolate, and food grade wax;

a handle having a connecting portion connected to said plug and said candy core and positioned in said plug-receiving opening and having a manually grippable handle portion extending downward from said connecting portion along said vertical axis; and
a substantially planar annular disk for abuttingly engaging and removably seating against said base and said lobes adjacent said plug, said disk defining a central axial hole for slidably receiving said handle portion and having an outer edge with a maximum span larger than said access opening but less than the maximum diameter of said symmetrical set of lobes to substantially minimize the interference with manually gripping of said manual grippable flange portions of said lobes, said disk being of a material selected from the group consisting of paper, paperboard, and plastic, and providing a removable closure member and seal for substantially closing said access opening and sealing said plug and said candy core within said shell.
The claims were rejected in view of thirteen references. The primary references, patents to Siciliano, Copeman, and Pooler, show ice cream or candy molded in a plastic, rubber or elastomeric mold. In Siciliano and Copeman the mold also serves as the product wrapper. In Siciliano the ice cream is poured into the mold, a stick is inserted, the ice cream is hardened, and a cardboard cover seals the area between the stick and the elastomeric wrapper. Copeman and Kuhlke show candy lollipops molded in elastomeric molds. Copeman states that the mold may take "varying shapes, such as in the form of fruit, or animals" and Kuhlke discusses the desirability of sealing candy from the outside air. In Siciliano, Copeman and Kuhlke, the mold is peeled from the confection prior to use.
The two Nolte patents teach that gripping flanges may be placed on an ice cream wrap

per to facilitate removal. Ahern and Knaust each show a disc-shaped seal or cover for a frozen confection. Ahern shows the cover in conjunction with ice cream on a stick.
Harris shows a hollow thumb-shaped lollipop into which the thumb is inserted, and Craddock shows a thumb-shaped confection supported on a disc-shaped handle; in both cases without the other elements shown by Gorman. Fulkerson shows a candy coating surrounding a block of ice cream, and a candy plug for retaining liquid syrup inside a cavity in the ice cream. Webster shows chewing gum entirely enclosing a liquid syrup product. Spiegel shows a chocolate layer having an alcohol diffusion barrier to plug the end of a plastic container of liqueur. Fulkerson,

Webster and Spiegel all suggest the greater appeal to consumers of providing two different components in the same confection.
The Board found that all of the features of Gorman's product were known to the art, and that various combinations of these elements existed in known similar structures. The Board concluded that the applicant's claimed combination was suggested by and would have been obvious in light of the references.

Discussion

A

Each element of the Gorman claims is in the prior art, separately or in sub-combination. Gorman argues that when it is necessary to combine the teachings of a large number of references in order to support a rejection for obviousness under 35 U.S.C. §103, this of itself weighs against a holding of obviousness.
[1] The criterion, however, is not the number of references, but what they would have meant to a person of ordinary skill in the field of the invention. In *Hybritech, Inc. v. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1383, 231 USPQ 81, 93 (Fed. Cir. 1986), *cert. denied,* 480 U.S. 947 (1987), the court held that a combination of about twenty references that "skirt[ed] all around" the claimed invention did not show obviousness. In other instances, on other facts, we have upheld reliance on a large number of references to show obviousness. Compare *In re Miller,* 159 F.2d 756, 758-58, 72 USPQ 512, 514-15 (CCPA 1947) (rejecting argument that the need for eight references for rejection supported patentability) with *Kansas Jack, Inc. v. Kuhn,* 719 F.2d 1144, 1149, 219 USPQ 857, 860 (Fed. Cir. 1983) (where teachings relied upon to show obviousness were repeated in a number of references, the conclusion of obviousness was strengthened). *See also, e.g., In re Troiel,* 274 F.2d 944, 947, 124 USPQ 502, 504 (CCPA 1960) (rejecting appellant's argument that combining a large number of references to show obviousness was "farfetched and illogical").
Determination of whether a new combination of known elements would have been obvious to one of ordinary skill depends on various facts, including whether the elements exist in "analogous art", that is, art that is reasonably pertinent to the problem with which the inventor is concerned. *In re Deminski,* 796 F.2d 436, 442, 230 USPQ 313, 315 (Fed. Cir. 1986). When the references are all in the same or analogous fields, knowledge thereof by the hypothetical person

of ordinary skill is presumed, *In re Sernaker,* 702 F.2d 989, 994, 217 USPQ 1, 5 (Fed. Cir. 1983), and the test is whether the teachings of the prior art, taken as a whole, would have made obvious the claimed invention. *See In re Young,* 927 F.2d 588, 591, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

When it is necessary to select elements of various teachings in order to form the claimed invention, we ascertain whether there is any suggestion or motivation in the prior art to make the selection made by the applicant. *Interconnect Planning Corp. v. Feil,* 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985). "'Obviousness can not be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination.'" *In re Bond,* 910 F.2d 831, 834, 15 USPQ2d 1566, 1568 (Fed. Cir. 1990) (quoting *Carella v. Starlight Archery and Pro Line Co.,* 804 F.2d 135, 140, 231 USPQ 644, 647 (Fed. Cir. 1986)).

The extent to which such suggestion must be explicit in, or may be fairly inferred from, the references, is decided on the facts of each case, in light of the prior art and its relationship to the applicant's invention. As in all determinations under 35 U.S.C. §103, the decisionmaker must bring judgment to bear. It is impermissible, however, simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps. *Interconnect Planning,* 774 F.2d at 1143, 227 USPQ at 551. The references themselves must provide some teaching whereby the applicant's combination would have been obvious.

B

Gorman argues that the references showing ice cream in a mold or wrapper on a stick and the references showing candy in a mold or wrapper on a stick are not analogous, for they require different conditions of production. However, the Copeman reference shows the close relationship of these arts, stating that his elastomeric mold may be used for "frozen confections and other solid confections". We conclude that the ice cream on a stick and candy on a stick arts are analogous, and that the Siciliano, Copeman, Pooler, and Kuhlke references show or suggest

Gorman's candy on a stick and covered with an elastomeric mold, for which the thumb-shape is shown by Harris or Craddock.

The suggestion of providing a layer of chewing gum, chocolate or the like, surrounding the candy core in the area not covered by the mold, to seal the candy and provide a second food product, is provided by Fulkerson, Webster, or Spiegel. The paper disc adjacent the base of the candy structure is shown in Ahern and Knaust. Harris and Craddock both show thumb-shaped candy. Gorman argues that the prior art does not suggest using the thumb-shaped cover as a toy after the candy is removed. However, Copeman states that his rubber mold may be used as a "toy balloon" after the candy is removed. Gorman argues that Craddock teaches away from the claimed invention because of Craddock's admonition that lollipops on sticks are dangerous to children. However, candy on a stick is too well known for this caution to contribute to unobviousness.

[2] Claim 16 recites details such as a "joint-shaped portion", a "finger nail portion", an "upper portion", a "lower portion" and a "convex back", as descriptive of the thumb shape. Such details are shown in the references and do not contribute to unobviousness. A claim that is narrowly and specifically drawn must nevertheless meet the requirements of §103:

The mere fact that a claim recites in detail all of the features of an invention (i.e., is a "picture claim") is never, in itself, justification for the allowance of such a claim.

Manual of Patent Examining Procedure, §706 (Rev. 6, Oct. 1987) at p. 700-6; *In re Romito,* 289 F.2d 518, 129 USPQ 359 (CCPA 1961) (rejecting a "picture claim").

[3] Applying the principles of *Graham v. John Deere & Co.,* 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), we discern all of the elements of claim 16, used in substantially the same manner, in devices in the same field of endeavor. The various elements Gorman combined: the molded lollipop with a chewing gum plug, with the mold serving as the product wrapper; and candy in the shape of a thumb; are all shown in the cited references in various sub-combinations, used in the same way, for the same purpose as in the claimed invention. The Board did not, as Gorman argues, pick and choose among isolated and inapplicable disclosures in the prior art. Rather, the claim elements appear in the prior art in the same configurations, serving the same functions, to achieve the results suggested in prior art. *In re Sernaker,* 702 F.2d at 994, 217 USPQ at 5. The large number of cited references does not negate the obviousness of the combination, for the prior art uses the various elements for the same purposes as they are used by appellants, making the claimed invention as a whole obvious in terms of 35 U.S.C. §103.

The Board's decision is *AFFIRMED.*

- End of Case -

In re Eli Lilly & Co.

U.S. Court of Appeals Federal Circuit
14 USPQ2d 1741

Decided April 30, 1990
No. 89-1076

Headnotes

PATENTS

1. Patentability/Validity - Obviousness - In general (§ 115.0901)

All evidence concerning obviousness must be considered anew, together with evidence submitted in rebuttal to prima facie showing of obviousness, after prima facie showing of obviousness is made; facts established by such rebuttal evidence must be evaluated together with facts on which prima facie conclusion of obviousness was reached, and not against conclusion itself.

2. Patentability/Validity - Obviousness - Relevant prior art (§ 115.0903)

Claimed method of enhancing weight gain in ruminant animals by oral administration of particular chemical compound is obvious in view of prior reference showing same chemical compound and its general use to enhance weight gain in animals, since, although unpredictability of biological properties of chemicals is entitled to some weight, reference in question specifically discloses compound of claims as having specific property of aiding weight gain in animals, including cattle and sheep, and therefore no significant aspect of invention is unexpected in view of prior art.

Particular patents - Chemical - Feed utilization improvers

3,794,732, Raun, ruminant feed utilization improvement, rejection of all claims on re-examination affirmed.

Case History and Disposition:

Appeal from the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences.

Reexamination of patent owned by Eli Lilly & Co. From rejection of all claims, patent owner appeals, and Hoffman-LaRoche Inc. intervenes. Affirmed.

Attorneys:

Donald R. Dunner, of Finnegan, Henderson, Farabow, Garrett & Dunner, Washington, D.C. (Herbert H. Mintz, Washington, with him on brief; Leroy Whitaker and Joseph A. Jones, Indianapolis, Ind., of counsel, also on brief), for appellant.

John H. Raubitschek, associate solicitor (Fred E. McKelvey, solicitor, with him on brief), for appellee PTO.

William H. Epstein, Nutley, N.J. (Christopher K. Hu and Patricia S. Rocha, Nutley; John C. Vassil, of Morgan & Finnegan, New York, N.Y., with him on brief), for intervenor Hoffman-La Roche Inc.

Judge:

Before Nichols, senior circuit judge, * and Newman and Michel, circuit judges.

Opinion Text

Opinion By:

Newman, J.

The decision of the United States Patent and Trademark Office Board of Patent Appeals and Interferences (the "Board"), rejecting claims 1-7, all of the claims on reexamination of United States Patent No. 3,794,732, inventor Arthur P. Raun, assignee Eli Lilly & Company (hereinafter "Lilly"), is affirmed.

Background

The Raun claims are directed to the method of using the chemical compound identified as X537A (common name "lasalocid") to enhance feed conversion efficiency in mature ruminant animals such as cattle and sheep. Claim 1 of the Raun patent is illustrative:

1. A method of increasing the efficiency of feed utilization of ruminant animals having a developed rumen function which comprises the oral administration to such animals of a

propionate-increasing amount of an antibiotic chosen from the group consisting of X537A and its physiologically acceptable esters and salts.

The Board held the claims unpatentable in terms of 35 U.S.C. §103, in view of certain Berger United States and foreign patents. All the Berger references discuss control of coccidiosis in fowl by treatment with X537A, and the weight gain effect of this treatment, as follows:

The active ingredient when orally administered to coccidiosis susceptible domestic fowl, particularly turkeys and chickens, as a component of feed, effectively controls the disease by either preventing it or curing it after it occurs. Furthermore, the treated fowl either maintain their weight or actually gain weight when compared to controls. Thus, the compositions of this invention not only control coccidiosis, but also, aid in improving the efficiency of conversion of feed to weight gains.

Berger U.S. Patent No. 3,719,753, column 5, lines 3-11. Berger's Southern Rhodesian patent No. 350/68/372 (June 30, 1962) includes the following disclosure, appearing as claim 23 of that patent:

A composition aiding in improving the efficiency of conversion of feed to weight gains in animals raised commercially for food purposes comprising ... antibiotic X-537A and pharmaceutically acceptable salts thereof.

The Southern Rhodesian patent describes (in claims 24-25) the dosages of X537A in these compositions, and also discloses (as the test of claims 26-29) an "animal feed composition" containing X537A "for aiding in improving the efficiency of conversion of feed to weight gains". The Berger references state that animals raised commercially for food purposes and subject to coccidiosis are "poultry ..., sheep, cattle, swine, etc."

The Berger data show an average weight gain of *Eimeria tanella* (coccidiosis) infected chickens treated with X537A that was greater than the weight gain of untreated infected chickens, Berger stating "[i]t should also be noted from the data in the table that the use of antibiotic as a coccidiostat does not substantially adversely affect the conversion of feed to weight gain" in the infected chickens. In the example for multiple *Eimeria* infections the average weight gain of treated infected chickens was shown as 108% and 105%, compared with untreated

uninfected controls at 100%. *Id.* at columns 9-10. Berger described the weight gain effect in

chickens as "greater than expected":
he antibiotic is ... further significant in causing greater than expected efficiency of conversion of feed to weight gain in the chickens[.]
Id. at column 10, lines 64-67. Berger does not present experimental data for any animal other than chickens.
In response to the examiner's rejection of the claims based on the Berger references, Lilly argued that Raun had shown certain unexpected results pertinent to weight gain in ruminant animals, and presented evidence and argument in support of patentability. The Board held, on the entire record, that the invention of the Raun claims would have been obvious in terms of Section 103.

Discussion

[1] The Board held that a *prima facie* case of obviousness was made by the Berger references. We agree, for the references show the same compound, X537A, as having the same general property of enhancing weight gain in animals. The burden thus was upon Lilly to come forward with evidence of the unobviousness of its claimed invention of the use of X537A to enhance weight gain in mature ruminant animals. After a *prima facie* case of obviousness has been made and rebuttal evidence submitted, all the evidence must be considered anew. *In re Piasecki,* 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984):
When prima facie obviousness is established and evidence is submitted in rebuttal, the decision-maker must start over.... An earlier decision should not, as it was here, be considered as set in concrete, and applicant's rebuttal evidence then be evaluated only on its knockdown ability. ... Facts established by rebuttal evidence must be evaluated along with the facts on which the earlier conclusion was reached, not against the conclusion itself.
(quoting *In re Rinehart,* 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976)).
Lilly provided expert opinions, documentary evidence and experimental data. Intervenor Hoffmann-La Roche ("Roche"), the assignee of the Berger United States patent, provided contrary analysis and argument.
Lilly argues that the most reasonable reading of the Berger references, including the Berger foreign patents, is as showing the use of X537A for treatment or prophylaxis of coccidiosis-infected chickens, and that it is unwarranted to read Berger's broad statements as teaching or suggesting the enhanced efficiency of weight gain in such animals as cattle and sheep. Lilly stresses that Berger does not provide data on the effects of feeding X537A to any

animal except chickens, and does not state that X537A should be fed to healthy cattle, or even to healthy chickens, in order to enhance their feed to weight gain efficiency. Lilly argues that at most Berger offers an invitation to experiment; that is, that the Berger teachings are in the discredited "obvious-to-try" category of disclosure insofar as they affect the Raun claimed invention.

An "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued. *See generally In re O'Farrell,* 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (defining obvious-to-try as when prior art gives "only general guidance as to the particular form of the claimed invention or how to achieve it").

Lilly presented the opinions of two persons, experienced in the field of animal husbandry, who stated that they viewed the Berger references as showing that the use of X537A to treat coccidiosis-infected chickens simply relieved the stress of the disease, thereby improving weight gain in chickens. One of these persons stated that because of the different digestive metabolisms of ruminants, as compared with chickens, the weight gain shown by Berger for chickens would not have led him to expect that X537A would be effective for weight gain purposes with cattle and sheep. Lilly presented experimental data that mature cattle (having a developed rumen function) experienced a higher percentage weight gain due to X537A, as compared with immature (unweaned, rumen function undeveloped) calves. Lilly argues that this result was unexpected, and overcomes any *prima facie* case of obviousness.

These arguments are countered by intervenor Roche. Roche stresses that the Berger foreign references describe X537A compositions for improving weight gain in animals grown commercially for food ("poultry ..., cattle, sheep, swine, etc."), and that the Southern Rhodesian patent disclosure is not limited to coccidiosis-infected animals or to chickens. Roche points to references showing compounds that improve weight gain in both poultry and cattle as evidence supporting obviousness of the Raun claimed invention.

Roche also challenges the significance of Lilly's data comparing the weight gains of calves and cattle, Roche arguing that Lilly's unweaned calves, even without treatment with X537A, were such highly efficient utilizers of their liquid feed that Lilly's comparisons are not probative of unexpected results with cattle. The date are shown in the following chart, accompanied by Lilly's interpretation thereof and Roche's counter-analysis.

	Calves		Steers	
	Control	X537A	Control	X537A
A. Av. daily intake (lbs)	3.04	3.05	16.76	15.77
B. Av. daily gain (lbs)	2.38	2.44	3.18	3.47
Lilly's Analysis:				
Intake/Gain (A/B ratio)	1.28	1.25	5.28	4.55
% Improvement over Control	--	2.3%	--	13.8%
Roche's Analysis:				
Gain/Intake (B/A %)	78.3%	80.0%	19.0%	22.0%
Improvement over Control	--	1.7%	--	3.0%
% of Maximum Improvement	--	7.8%	--	3.7%

Lilly's expert explained that the observed improvement for the calves was not significant, but that the improvement for steers was significant, and that the difference from calves was unexpected. Roche asserts that because calves are already so efficient in utilization of feed, the treatment with X537A actually had a greater proportional impact on the calves than on the steers.

The Board held that Lilly's evidence of improved feed efficiency in steers as compared with calves did not outweigh the evidence of the Berger teachings that the conversion of feed to weight gains is improved in animals raised commercially for food, including cattle.

Each side asserts that its position is required by precedent. Lilly cites *In re Yates,* 663 F.2d 1054, 1056-57, 211 USPQ 1149, 1151 (CCPA 1981) (process patentable based on previously unknown relationship among variables); *In re Orfeo,* 440 F.2d 439, 442, 169 USPQ 487, 489 (CCPA 1971) (method of use patentable based on unexpected superiority in known properties of known compounds); and *In re Chupp,* 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987) (new compound patentable based on unexpected results in one of a spectrum of common properties), in support of its position that the difference between weight gains of steers and calves establishes patentability of the Raun claims. Rejecting these cases as inapt on their facts, the Commissioner states that the Board correctly relied on *In re Nolan,* 553 F.2d 1261, 1267, 193 USPQ 641, 645 (CCPA 1977) (improvement in gaseous discharge device and process

unpatentable because although unexpected results were shown in some features, the results were not unexpected in the most significant feature).

In *Yates* the prior art showed the same chemical process as that of the applicant for oxidizing an olefin to an unsaturated aldehyde, but contained no express teaching of the specific relationship between process variables that was demonstrated by the applicant. 663 F.2d at 1057, 211 USPQ at 1151. The court held that the relationship was unobvious from the prior art, and authorized claims specific to the combination of process variables.

In *Chupp* the claimed invention was a new herbicidal compound that was within a known class of herbicides. The claimed compound was the homolog (*i.e.,* differing by a methylene (-CH_2) group) of a known herbicidal compound. Chupp submitted data showing that his new compound had selective herbicidal activity as to specific crops and weeds that was at least five times greater than that of the known homolog. The court held Chupp's new compound to be patentable because it possessed unexpectedly superior herbicidal properties compared to the prior art compound. *Chupp,* 816 F.2d at 646-47, 2 USPQ2d at 1439-40.

In *Orfeo* the references showed the use of certain halocarbons as refrigerants, and also showed the use of mixtures of halocarbons for this purpose. Orfeo's claimed invention was the azeotrope of two of these halocarbons, which formed a refrigerant that had an unexpectedly lower power requirement than either of the components alone. The court explained that "even though the claimed invention involves the use of a known compound in a known process it is still unobvious

to one of ordinary skill in the art because of the new and unexpected results and effects achieved." 440 F.2d at 442, 169 USPQ at 489.

The Board held that these authorities were factually distinguished from the Raun situation, or simply limited to their facts. The Board cited *Nolan, supra,* as more closely analogous to the factual situation at bar. In *Nolan* the applicant claimed the use of a specific ionizable noble gas composition as an improvement in a gaseous discharge display/memory device. Although the prior art showed the use of similar noble gas compositions in gaseous discharge devices, the applicant argued that his specific composition had unexpected performance benefits in memory devices. The court found that the most significant of Nolan's alleged performance benefits

followed from the known ionization potential of the gas, and thus was taught in and expected from the prior art, whereas only some less significant benefits were shown to be unexpected from the prior art. The court held that the evidence of obviousness outweighed the evidence of unobviousness. 553 F.2d at 1267, 193 USPQ at 645.

Analysis

Review of the authorities relied on by both sides shows the absence of detailed all-purpose criteria for applying the law of obviousness to every factual situation. No one precedent or rationale can be controlling in all possible areas of human creativity. See the extensive review of cases in *In re Dillon,* 892 F.2d 1554, 13 USPQ2d 1337 (Fed. Cir. 1989), illustrating the variety of factors that courts have considered in deciding the question of obviousness of particular inventions. The value of the exceedingly large body of precedent wherein our predecessor courts and this court have applied the law of obviousness to particular facts, is that there has been built a wide spectrum of illustrations and accompanying reasoning, that have been melded into a fairly consistent application of law to a great variety of facts. The uniform application of the law of "obviousness" is essential to the commercial incentive that is the core of the patent system. The obligation of the decisionmaker is to apply the law consistently to the evidence for each new invention. All relevant facts must be considered, while recognizing that it is inappropriate to "squeez[e] new factual situations into preestablished pigeonholes." *Yates,* 663 F.2d at 1056 n.4, 211 USPQ at 1151 n.4.

In each of *Yates, Orfeo, Chupp,* and *Nolan,* the prior art showed the same general composition or method as did the applicant. In each of these cases the applicant referred to comparative data for the purpose of demonstrating that the claimed invention would not have been obvious to a person of ordinary skill in the field of the invention. The substance of these comparisons varied with the nature of each invention. In *Yates* the data were contained in the application as filed, and the court held that in considering these data the PTO had not made a *prima facie* case of obviousness. In *Chupp* and *Orfeo* the applicant's additional evidence of superior or unexpected results in the claimed inventions, as compared with similar properties and uses shown in the prior art, was held to outweigh the evidence of obviousness; whereas in *Nolan* the evidence of superior results was held inadequate to outweigh the evidence of obviousness.

[2] In the case before us, the prior art showed the compound X537A and its general use to enhance weight gain in animals. 1 The Board placed great weight on Berger's statements that

X537A compositions "aid in improving the efficiency of conversion of feed to weight gains in animals raised commercially for food purposes," and that such animals include "poultry ..., sheep, cattle, swine, etc." This general teaching was not shown to be incorrect.

We have considered Lilly's argument and supporting documents that X537A is of commercial importance and superior to other products. In this case, however, Berger disclosed the same product, X537A, for the same use that Raun seeks to claim. The Berger disclosure does not merely invite experimentation, for Berger states that this specific product has the specific property of aiding weight gain in animals, naming cattle and sheep. *See O'Farrell,* 853 F.2d at 901, 7 USPQ2d at 1679 ("Thus, the prior art explicitly suggested the substitution that is the difference between the claimed invention and the prior art, and presented preliminary evidence suggesting that the method could be used to make proteins.") Although we recognize and give weight to the unpredictability of biological properties, in Raun's

case the prior art teaches the claimed use with specificity.

In view of all of the evidence of record, we think the Board was correct in holding that the evidence of unobviousness did not outweigh the clear teaching of the prior art of the property and use of "increasing the efficiency of feed utilization in ruminant animals", quoting from Raun's claim 1. Unlike *Yates,* Raun is not claiming a narrow improvement limited to details not shown in the prior art. Unlike *Chupp,* Raun has not shown unexpected superiority over the property taught in the prior art. Unlike *Orfeo,* Raun has not shown that his claimed use with ruminants achieves unexpected results compared with the prior art disclosure of the same use with the same animals. Like *Nolan,* Raun has not shown that a significant aspect of his claimed invention is unexpected in light of the prior art.

We conclude that the Board correctly held that Raun's claimed invention would have been obvious in terms of 35 U.S.C. §103.

AFFIRMED

Footnotes

Footnote 1. This is the distinction from the decision in *Eli Lilly & Co. v. A.H. Robins Co.*, 228 USPQ 757 (E.D. Va. 1985), *aff'd,* 790 F.2d 95 (Fed. Cir.) (table), *cert. denied,* 479 U.S. 827 (1986). In the *Robins* case, according to the published opinion, the claimed use of salinomycin to enhance weight gain in ruminants was not taught or suggested in the prior art, 228 USPQ at 759, unlike the facts of the case at bar.

Footnote *. The Honorable Philip Nichols, Jr., who died on January 26, 1990, did not participate in this decision.

- End of Case -

Merck & Co. Inc. v. Biocraft Laboratories Inc. (CA FC) 10 USPQ2d 1843

Merck & Co. Inc. v. Biocraft Laboratories Inc.

U.S. Court of Appeals Federal Circuit
10 USPQ2d 1843

Decided May 10, 1989
No. 88-1513

Headnotes

PATENTS

1. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Invention is merely "obvious to try" if prior art gives either no indication of which parameters are critical or no direction as to which of many possible choices is likely to be successful.

2. Patentability/Validity -- Obviousness -- Relevant prior art (§ 115.0903)

Claims for diuretic formulations are rendered obvious by prior art patent which teaches genus of which claims at issue are species, and which instructs artisan that any of 1,200 disclosed combinations will produce diuretic formulation with desirable sodium and potassium eliminating properties, even though prior art reference does not highlight either amiloride or hydrochlorothiazide, since, under 35 USC 103, fact that specific embodiment is taught to be preferred is not controlling, and even though prior art patent does not describe effects of combined drug on sodium and potassium excretion, since mere absence from prior art of teaching or limitation recited in patent at issue is insufficient for finding of non-obviousness.

3. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Synergism is not requirement for nonobviousness, but inventor who seeks to distinguish claims from prior art by introducing evidence of unexpected synergistic properties must at least demonstrate effect greater than sum of several effects taken separately.

REMEDIES

4. Monetary -- Attorney's fees; costs -- Patents (§ 510.0905)

Appellee which cited in its brief portions of record not specifically relied upon has disregarded spirit, if not letter, of Fed. Cir. R. 30(b), and thus should be taxed with full cost of preparing appendix.

Particular patents -- Chemical -- Diuretic formulations

3,781,430, Cragoe, potassium conserving diuretic co-administered with potassium excreting diuretic to avoid hypokalemia in patients, invalid.

Case History and Disposition:

Appeal from the U.S. District Court for the District of New Jersey, Politan, J.

Merck & Co. Inc. brought patent infringement action against Biocraft Laboratories Inc. From federal district court decision holding patent to be valid and enforceable, defendant appeals finding of validity. Reversed; Bissel, J. dissents in separate opinion.

Attorneys:

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Judge:

Before Bennett, senior circuit judge, and Bissell and Mayer, circuit judges.

Opinion Text

Opinion By:
Mayer, J.

Merck & Co., Inc. sued Biocraft Laboratories, Inc. for infringement of its patent, U.S. Patent No. 3,781,430. The United States District Court for the District of New Jersey held that Biocraft failed to show by clear and convincing evidence that the patent was invalid or unenforceable, and enjoined Biocraft from commercially making, using, and selling the claimed diuretic formulations. *Merck & Co., Inc. v. Biocraft Laboratories, Inc* ., 690 F.Supp. 1376 (D.N.J. 1988). Biocraft appeals only the validity aspect of the judgment, arguing that the claimed combinations would have been obvious under 35 U.S.C. §103. We agree and accordingly reverse the judgment of the district court.

Background

The '430 Patent :

In relevant part, U.S. Patent No. 3,781,430 (the '430 patent), assigned to Merck, claims various "Diuretic Formulations." Inducing diuresis (increased urine excretion) or saluresis (increased electrolyte, particularly sodium, excretion), or both, diuretics are useful in the treatment of cardiovascular and renal diseases. Although the therapeutic effects of diuretics are often life-saving, many cause hypokalemia, the excessive excretion of potassium ions, a condition manifested by severe muscle weakness and physical exhaustion.
In the formulations claimed in the '430 patent, amiloride hydrochloride (amiloride), a known "potassium conserving" diuretic (induces sodium, but not potassium, excretion), is combined with hydrochlorothiazide, a known "potassium excreting" diuretic (induces both sodium and potassium excretion). As stated in the specification, the objective of co-administration is to reduce the amount of potassium ions eliminated, without reducing the amount of sodium ions eliminated. The inventor also reports that co-administration results in a "medically . . . synergistic therapeutic accomplishment" because "more sodium ions are eliminated than would be forecast from a knowledge of the natriuretic [sodium excreting] effects of the individual drugs."
The '430 patent contains six claims. The parties agree, however, that all of the claims stand or

fall with claims 2 and 3. Claim 1, on which claim 2 depends, and claims 2 and 3 provide as follows:

1. A composition for oral administration comprising amiloride hydrochloride and

hydrochlorothiazide, wherein the ratio of amiloride hydrochloride to hydrochlorothiazide ranges from about 1:1 to 1:10 by weight of the composition.

2. A composition according to claim 1 wherein amiloride hydrochloride and hydrochlorothiazide are combined at a ratio of 1 to 10 by weight.

3. A composition for oral administration which comprises 5 mg. of amiloride hydrochloride and 50 mg. of hydrochlorothiazide.

The Infringement Suit :

Merck's suit against Biocraft was prompted by Biocraft's filing of an abbreviated new drug application (ANDA) with the Food & Drug Administration (FDA) for a generic version of Merck's amiloride/hydrochlorothiazide combination, "Moduretic." The Drug Price Competition and Patent Term Restoration Act of 1984 permits the filing if the generic manufacturer can certify its belief that the patent is invalid or will not be infringed by its proposed manufacture, use or sale of the drug, and notifies the patent owner of the reasons for its belief. 21 U.S.C. §355(b)(2)(A)(iv) and (3). However, under 35 U.S.C. §271(e)(2), the filing is a technical act of infringement, so infringement is not an issue in this case. If a patent owner brings an infringement suit, the FDA cannot approve the ANDA unless the patent is declared invalid or not infringed. 21 U.S.C. §355(c)(3)(C).

At trial, Biocraft argued that the '430 patent was invalid for obviousness under 35 U.S.C. §103, and unenforceable because of inequitable conduct. The district court ruled against Biocraft on both counts. Biocraft predicated its section 103 argument on two prior art patents and on prior art relating to spironolactone and triamterene, diuretics that, like amiloride, are potassium conserving. Refreshingly, Biocraft challenges the judgment of the district court only as to obviousness, and restricts its arguments to the teachings of U.S. Patent No. 3,313,813 (the '813 patent), also assigned to Merck.

The '813 patent discloses various (3-amino-5, 6-dissubstituted-pyrazinoyl) guanidines, one of

which is amiloride (claim 11). Per the specification, the claimed compounds are effective diuretic and natriuretic agents. Moreover, the '813 patent teaches that guanidines "selectively enhance the excretion of sodium ions without causing an increase in excretion of potassium ions," and "are useful in combination with other classes of diuretic agents to prevent the loss of potassium which the other diuretics otherwise would cause to be eliminated." Hydrochlorothiazide is identified as an example of a potassium excreting diuretic with which the claimed compounds can be combined.

The '813 patent therefore teaches a genus of which the claims of the '430 patent are a species. The question addressed in the district court was whether the '813 patent taught the specific 1:10/5 mg:50 mg, "medically synergistic," amiloride/hydrochlorothiazide, combination claimed in the '430 patent. Biocraft argued that the claimed combination was taught because both amiloride and hydrochlorothiazide were highlighted in the '813 patent. Moreover, Biocraft pointed out that the Patent and Trademark Office considered the claimed combination *prima facie* obvious, and allowed the '430 patent only after Merck presented evidence allegedly demonstrating a natriuretic synergism produced by the combination. Asserting that the alleged synergistic effect is not exhibited by the 5mg:50 mg combination, and that therefore, the effect, even if produced, is not commensurate in scope with the claims, Biocraft argued that neither the purported effect nor the dosage limitations distinguish the claims from the disclosure of the '813 patent. The district court, however, was not persuaded, and held that Biocraft failed to carry its burden of proving the obviousness of the claims. This appeal followed.

Discussion

The district court found that the combination of amiloride and hydrochlorothiazide was disclosed in the '813 patent. 690 F.Supp. at 1383. Further finding that more than 1200 combinations are disclosed, and that neither amiloride nor hydrochlorothiazide are highlighted as preferred embodiments in the '813 patent, however, the district court concluded that the combinations claimed in the '430 patent would merely be "obvious to try," and therefore not barred by 35 U.S.C. §103. We do not quarrel with the factual findings of the district court, but we believe its conclusion that obviousness had not been proven is incorrect as a matter of law.

[1] An invention is "obvious to try" "where the prior art [gives] either no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful." *In re O'Farrell* , 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). This

is not the situation here. The '813 patent expressly teaches "that when co-administered with other diuretic agents known to enhance the limitation of potassium ions along with sodi

um ions, the novel pyrazinoylguanidines of this invention will reduce the excretion of potassium ions and thus overcome this undesirable property of other diuretic agents." As is apparent, "success" is not dependent upon random variation of numerous parameters. On the contrary, the '813 patent instructs the artisan that any of the 1200 disclosed combinations will produce a diuretic formulation with desirable sodium and potassium eliminating properties.

[2] That the '813 patent discloses a multitude of effective combinations does not render any particular formulation less obvious. This is especially true because the claimed composition is used for the identical purpose taught by the prior art. *See In re Corkill* , 771 F.2d 1496, 1500, 226 USPQ 1005, 1008 (Fed. Cir. 1985) (obviousness rejection of claims affirmed in light of prior art teaching that "hydrated zeolites will work" in detergent formulations, even though "the inventors selected the zeolites of the claims from among 'thousands' of compounds"); *In re Susi* , 440 F.2d 442, 445, 169 USPQ 423, 425 (CCPA 1971) (obviousness rejection affirmed where the disclosure of the prior art was "huge, but it undeniably include[d] at least some of the compounds recited in appellant's generic claims and it is of a class of chemicals to be used for the same purpose as appellant's additives").

Merck imputes undue significance to the district court's finding that neither amiloride nor hydrochlorothiazide are highlighted in the '813 patent. The description of "specific preferences in connection with a generic formula" is determinative in an analysis of anticipation under 35 U.S.C. §102. *In re Petering* , 301 F.2d 676, 681, 133 USPQ 275, 279 (CCPA 1962); *see also In re Schaumann* , 572 F.2d 312, 315, 316, 197 USPQ 5, 8, (CCPA 1978) ("the disclosure of a chemical genus . . . constitute[s] a description of a specific compound" within the meaning of section 102(b) where the specific compound falls within the ambit of a "very limited number of compounds"). But in a section 103 inquiry, "the fact that a specific [embodiment] is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be considered." *In re Lamberti* , 545 F.2d 747, 750, 192 USPQ 278, 280 (CCPA 1976).

Merck also attributes determinative importance to the district court's finding that the '813 patent

does not describe "the effects that the combined drug would have on sodium excretion, potassium excretion and ratio of sodium excretion to potassium excretion" that are described in the specification of the '430 patent, 690 F.Supp. at 1383, nor does it "teach the specific ratios of the combinations" disclosed in the '430 patent, *id* . But, the mere absence from the prior art of a teaching or a limitation recited in the patent at issue is insufficient for a conclusion of nonobviousness. Unlike a section 102 defense which requires that a single reference described each and every element of a claimed invention, *Structural Rubber Products Co. v. Park Rubber Co* ., 749 F.2d 707, 715, 223 USPQ 1264, 1270 (Fed. Cir. 1984), "the question under 35 USC 103 is not merely what the references expressly teach but what they would have suggested to one of ordinary skill in the art at the time the invention was made." *In re Lamberti* , 545 F.2d at 750, 192 USPQ at 280. That this distinction was missed is evident from the district court's erroneous assertion that because the '813 patent " 'suggests,' " but does not " 'teach' " the combinations claimed in the '430 patent, obviousness had not been proven. 690 F.Supp. at 1383.

As prescribed by section 103, the proper focus of an obviousness inquiry is on whether "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. . . ." Merck argues that the dosages and ratios of claims 2 and 3, and the properties of the 5 mg of amiloride and 50 mg of hydrochlorothiazide combination patentably distinguish the claims of the '430 patent from the teaching of the '813 patent. Relying on evidence allegedly demonstrating that the properties Merck posits are not exhibited by the 5 mg/5O mg combination, Biocraft insists that the claims are invalid under section 103; but this begs the question. Even if Merck's representations are accepted, the issue remains whether the asserted properties and proportions impart patentability to the claimed inventions, or whether the inventions as a whole would have been obvious to one skilled in the art.

Merck offers several theories to bolster the claimed combinations' purportedly nonobvious properties. In response to the examiner's rejection of the claims on the ground that the amiloride/hydrochlorothiazide combination was *prima facie* obvious, Merck said that the co-administration of the two diuretics achieved a "medically synergistic" result. This apparently convinced the examiner, but it should not have.

[3] "The patent law 'allows the inventor to be his own lexicographer,' " *Loctite Corp. v. Ultraseal Ltd* ., 781 F.2d 861, 867, 228 USPQ 90, 93 (Fed. Cir. 1985) (quoting

Autogiro Co. of America v. United States , 384 F.2d 391, 397, 155 USPQ 697, 702 (Ct. Cl. 1976)), but he may not compose his own standards of patentability. Synergism is not a requirement of nonobviousness. *Gardner v. TEC Sys. Inc* ., 725 F.2d 1338, 1349, 220 USPQ 777, 786 (Fed. Cir. 1983) (in banc). But when an inventor tries to distinguish his claims from the prior art by introducing evidence of unexpected "synergistic" properties, the evidence should at least demonstrate "an effect greater than the sum of the several effects taken separately." *Sakraida v. Ag Pro, Inc* ., 425 U.S. 273, 282, 189 USPQ 449, 453 (1976). It is insufficient that, as Merck defines "medical synergism" in the specification of the '430 patent, the "two drugs react favorably."

At trial, Merck altered its approach and tried to show that a greater than additive effect, in terms of sodium excretion, is obtained when amiloride and hydrochlorothiazide are co-administered. It failed. The district court said only that amiloride and hydrochlorothiazide can be co-administered "without a reduction in the amount of sodium ions that are eliminated," 690 F.Supp. at 1378, and that the effect of co-administration as set forth in the specification of the '430 patent was not described in the '813 patent, 690 F.Supp. at 1383. Merck's proposed finding that an unexpectedly strong natriuretic effect occurs was not adopted by the district court. Moreover, on appeal, Merck says only that the evidence at trial "demonstrated that the combination causes more sodium excretion than 50 mg of hydrochlorothiazide alone". This is quite different from the proposition advanced at trial, and imparts no patentability to the claimed inventions.

Given the prior art teaching that both amiloride and hydrochlorothiazide are natriuretic, it is to be expected that their co-administration would induce more sodium excretion than would either diuretic alone. *See In re Crockett* , 279 F.2d 274, 276, 126 USPQ 186, 188 (CCPA 1960) (the "joint use [of magnesium oxide and calcium carbide] is not patentable" where the prior art teaches "that both magnesium oxide and calcium carbide, individually, promote the formation of a nodular structure in cast iron, and it would be natural to suppose that, in combination, they would produce the same effect and would supplement each other"). Indeed, the inventor named on both the '813 and the '430 patents, so testified. When asked: "Isn't it also normal when you administer a potassium sparing compound along with hydrochlorothiazide a period of time, that there would be some increase in the amount of sodium excretion?", he responded: "That is a

possibility. That is not an assured consequence." But, "absolute predictability of success" is not the criterion; "[f]or obviousness under §103, all that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d at 903, 7 USPQ2d at 1681. When further questioned on the point, the inventor indicated that his uncertainty inhered not in the fact that an increase was to be expected, but only in the magnitude of the increase. This, he testified, "Depends on the amount of potassium sparing compound that you have."

Merck's further contention that the claimed inventions as a whole would not have been obvious because of the recited dosage limitations is equally unpersuasive. "Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Patentability may be imparted, however, if the results achieved at the designated concentrations are "unexpectedly good." *In re Antonie*, 559 F.2d 618, 620, 195 USPQ 6, 8 (CCPA 1977). As discussed above, this is not the situation here. Assuming, as Merck alleges, that "[t]he specific combination of 5 mg of amiloride and 50 mg of hydrochlorothiazide results in no decrease and indeed an increase in sodium excretion over hydrochlorothiazide alone," this was to be expected from the known natriuretic properties of the two diuretics.

The evidence at trial showed that, though requiring time and care, the experimentation needed to arrive at the claimed dosages was nothing more than routine. "Patentability shall not be negatived by the manner in which the invention was made." 35 U.S.C. §103. But the converse is equally true: patentability is not imparted where "the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in light of the prior art." *In re Dow Chemical Co*., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

This is precisely the situation here. Merck's expert, the inventor of hydrochlorothiazide, and the witness that the district court found "most closely represents the hypothetical person skilled in the art," 690 F.Supp. at 1382, testified that the dose response and compatability procedures followed by Merck were those that "all pharmaceutical companies [follow] whenever they determine the appropriate dose; the minimal dose and the appropriate dose." After describing the animal and human stud

ies that were conducted, he explained: "That is the way it is done not only with amiloride, but with any other drug that you are testing." Reached by means of routine procedures, and producing only predictable results, the recited dosages therefore do not distinguish the claims of the '430 patent from the amiloride/hydrochlorothiazide combination that the district court properly found was disclosed in the '813 patent. *Cf. United States v. Telectronics, Inc* ., 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) (specification is enabling in part because those skilled in the art would know how to conduct a dose response study to determine the appropriate amounts to be used). *

Costs

[4] Biocraft moves to tax Merck the full cost of printing the appendix prepared for this appeal. Biocraft states that Merck disregarded "the spirit, if not the letter, of Fed.Cir.R. 30(b) by citing in its brief portions of the record not specifically relied upon." We agree. Our review of the matter shows, for example, that Merck generally cited hundreds of pages of the record in its preliminary introduction of the witnesses, but relied only on a small fraction of those pages in the remainder of its brief; lengthy scholarly articles were reproduced in their entirety but not relied upon by Merck; and a fully reproduced 700-plus page book, though mentioned once by Merck, was similarly not relied upon.
Accordingly, we grant Biocraft's motion. When assessing costs, the Clerk will tax Merck with the full cost of printing the appendix.

Conclusion

The judgment of the district court is reversed.

REVERSED

Footnotes

Footnote *. The district court also referred to evidence of Moduretic's commercial success. Commercial success is an indication of nonobviousness that must be considered in a patentability

analysis, *Graham v. John Deere Co* ., 383 U.S. 1, 17, 148 USPQ 459, 467 (1966), but in the circumstances of this case, where it is the only such indication, it is insufficient to render Merck's claimed invention nonobvious. *See W.L. Gore & Assoc., Inc. v. Garlock, Inc* ., 721 F.2d 1540, 1555, 220 USPQ 303, 314 (objective evidence of nonobviousness "may in a given case be entitled to more weight or less, depending on its nature and its relationship to the merits of the invention").

Dissenting Opinion Text

Dissent By:

Bissell, J., dissenting.

I would affirm the district court's decision that the claims at issue in United States Patent No. 3,781,430 ('430) were not shown to have been obvious under 35 U.S.C. §103 (1982). The district court concluded that a combination of amiloride and hydrochlorothiazide as claimed in the '430 patent was merely "obvious to try" based on the prior art. *Merck & Co., Inc. v. Biocraft Laboratories, Inc* ., 690 F.Supp. 1376, 1381 (D. N.J. 1988) (citing *In re Geiger* , 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987) (rejecting "obvious to try" as the standard for determining obviousness)).

Obviousness, a question of law, is based on underlying factual inquiries. *See Uniroyal, Inc. v. Rudkin-Wiley Corp* ., 837 F.2d 1044, 1050, 5 USPQ2d 1434, 1438 (Fed. Cir.), *cert. denied* , 109 S.Ct. 75 (1988). The parties agree that the closest prior art to the '430 patent is United States Patent No. 3,313,813 ('813). Additionally, the majority opinion *does not* "quarrel with the factual findings of the district court." In pertinent part the district court stated:

The '813 patent discloses appropriately 120 pyrazinoylguanidine compounds. There is no indication in the patent that amiloride is the preferred compound. Thus, a person skilled in the art, would not be taught by the '813 patent that amiloride and hydrochlorothiazide should be combined to produce the effects as set forth in the '430 patent. The '813 patent does not describe or forecast the effects that the combined drug would have on sodium excretion, potassium excretion and ratio of sodium excretion to potassium excretion. A composition must be assessed for obviousness only after consideration of its chemical structure as well as its pharmaceutical and biological properties. In short, while the '813 patent "suggests" exploration of combinations

of potassium sparing guanidine with potassium losing diuretics, such as hydrochlorothiazide, it does not "teach" the combinations claims in the '430 patent.
Nor does it teach the specific ratios of the combinations as outlined in Claims 2, 3, 5 and 6 of the '430 patent. Those claims are sufficiently non-obvious so as to sustain the validity of the patent. Since the '813 patent discloses in excess of 120 pyrazinoylguanidine and 10 possible potassium losing diuretics, there are more than 1200 possible combinations, of which the combination of Amiloride and Hydrochlorothiazide would be one. And there is no indication in the '813 patent as to the preference for amiloride as opposed to any

other pyrazinoylguanidine compound, nor hydroclorothiozide [sic] as opposed to other diuretics. Nor is there any hint as to the proportions that would be contained in the mixture. Again, while the '813 patent might titillate one's desire to experiment, it clearly does not teach and thereby make obvious the claims as outlined in Claims 2, 3, 5 and 6 of the '430 patent.
Merck, 690 F.Supp. at 1383-84.
The majority opinion incorrectly states that the district court found "the combination of amiloride and hydrochlorothiazide was disclosed in the '813 patent." The district court, in fact, found that the '813 patent disclosed "in excess of 120 pyrazinoylguanidine and 10 possible potassium losing diuretics, [resulting in] more than 1200 possible combinations, of which the combination of Amiloride and Hydrochlorothiazide would be one." *Id*. The '813 patent does not disclose a diuretic composition containing amiloride and hydrochlorothiazide.
After examining the scope and content of the prior art, the district court found that the '813 patent does not (1) teach one of ordinary skill in the art a preference for amiloride, hydrochlorothiazide, or their combination, (2) "describe or forecast the effects that the combined drug would have on sodium excretion, potassium excretion and ratio of sodium excretion to potassium excretion," and (3) teach the specific ratio limitations of the claims in suit. *Id*. Additionally, the district court determined that the '813 patent only suggests "exploring" combinations of potassium sparing and potassium losing diuretics, and that the prior art does not teach one of ordinary skill what is claimed in the '430 patent. *Id*. I agree. The claimed invention would not have been obvious in view of prior art that does no more than suggest experimenting with over 1200 combinations to come up with the right one.

The meaning to one of ordinary skill in the art of the '813 patent was extensively explored at trial. Based upon this testimony, the district court found that Merck's expert, the inventor of hydrochlorothiazide, "most closely represent[ed] the hypothetical person skilled in the art." *Id*. at 1382. After reviewing the prior art, Merck's expert testified that in 1966 the combination of amiloride and hydrochlorothiazide would not have been obvious, and if combined, he would not have expected the results achieved.

In examining secondary considerations, the district court found "uncontroverted evidence" of commercial success, *id*. at 1385 n.4, but made no express findings on unexpected results. Yet the majority, after extended discussion, finds no unexpected results. Absent more definitive findings by the district court, the basis for the majority's statement escapes me.

Hindsight is not the standard for determining obviousness. *See, e.g., Uniroyal*, 837 F.2d at 1050-51, 5 USPQ2d at 1438. Bits and pieces of the invention claimed in the '430 patent can be pointed to in the prior art, but only if one is armed with hindsight knowledge. *See id*. (stating that hindsight reconstruction using the claimed invention as a blueprint is improper). The majority's opinion does not disturb the district court's factual findings. Based on these findings, I cannot agree with the majority's conclusion that the claims of the '430 patent would have been obvious. Accordingly, I would affirm the district court's judgment.

- End of Case -

In re O'Farrell

U.S. Court of Appeals Federal Circuit
7 USPQ2d 1673

Decided August 10, 1988
No. 87-1486

Headnotes

PATENTS

1. Patentability/Validity -- Obviousness -- Evidence of (§ 115.0906)

Applicants' method of producing predetermined protein in stable form in host species of bacteria through genetic engineering is obvious within meaning of 35 USC 103 since reference, authored by two of three patent applicants and published more than one year prior to patent application date, contained detailed enabling methodology for practicing claimed invention, suggestion for modifying prior art to practice claimed invention, and evidence suggesting that invention could

be successful, and reference thus rendered invention obvious to those of ordinary skill in art at time invention was made.

2. Patentability/Validity -- Obviousness -- Evidence of (§ 115.0906)

Experimenters' use of heterologous gene coded for ribosomal RNA, which is not ordinarily translated, rather than gene coded for predetermined protein, in plasmid cloning vector for introduction into host bacteria in genetic engineering experiment, does not require finding that applicant's claimed method of producing predetermined protein in host bacteria through genetic engineering was not obvious in view of published paper describing experiment, particularly observation that hybrid messenger RNA produced by experiment was apparently translated into protein, since it would have been obvious and reasonable to conclude from such observation that if gene coded for ribosomal RNA produced "junk" or "nonsense" protein, then use of gene coded for predetermined protein would result in production of "useful" protein, as application claims.

3. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Rejection of patent application cannot be overturned on ground that examiner and Board of Patent Appeals and Interferences applied impermissible "obvious to try" standard, since assignment of error for application of such standard usually occurs when invention is made by varying all parameters or trying each of numerous choices until successful without indication in prior art as to which parameters were critical or which choices were likely to be successful, or when invention is made by exploring promising new technology or general approach with only general guidance from prior art as to particular form of claimed invention or how to achieve it, and since neither situation is present in instant case.

4. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Finding of obviousness under 35 USC 103 requires only that prior art reveal reasonable expectation of success in producing claimed invention, rather than absolute prediction of such success.

Case History and Disposition:

Appeal from decision of Patent and Trademark Office, Board of Patent Appeals and Interferences.

Patent application, serial no. 180,424, filed by Patrick H. O'Farrell, Barry O. Polisky, and David H. Gelfand. From decision of Board of Patent Appeals and Interferences affirming final rejection of application on grounds of obviousness, applicants appeal. Affirmed.

Attorneys:

J. Bruce McCubbrey of Fitch, Even, Tabin & Flannery (Virginia H. Meyer, with them on brief), San Francisco, Calif., for appellant.

Harris A. Pitlick, associate solicitor, Patent and Trademark Office (Joseph F. Nakamura, solicitor and Fred E. McKelvey, deputy solicitor, with him on brief), for appellee.

Judge:

Before Markey, chief judge, and Rich and Nies, circuit judges.

Opinion Text

Opinion By:

Rich, J.

This appeal is from the decision of the United States Patent and Trademark Office Board of Patent Appeals and Interferences (board) affirming the patent examiner's final rejection of patent application Serial No. 180,424, entitled "Method and Hybrid Vector for Regulating Translation of heterologous DNA in Bacteria." The application was rejected under 35 USC 103 on the ground that the claimed invention would have been obvious at the time the invention was made in view of a published paper by two of the three coinventors, and a publication by Bahl, Marians & Wu 1 *Gene* 81 (1976) (Bahl). We affirm.

The claimed invention is from the developing new field of genetic engineering. A broad claim on appeal reads:

Claim 1. A method for producing a predetermined protein in a stable form in a transformed host species of bacteria comprising, providing a cloning vector which includes at least a substantial portion of a gene which is indigenous to the host species of bacteria and is functionally transcribed and translated in that species, said substantial portion of said indigenous gene further including the regulatory DNA sequences for RNA synthesis and protein synthesis but lacking the normal gene termination signal, and linking a natural or synthetic heterologous gene encoding said predetermined protein to said indigenous gene portion at its distal end, said heterologous gene being in proper orientation and having codons arranged in the same reading frame as the codons of said indigenous gene so that readthrough can occur from said indigenous gene portion into said heterologous gene in the same reading frame, said heterologous gene portion further containing sufficient DNA sequences to result in expression of a fused protein having sufficient size so as to confer stability on said predetermined protein when said vector is used to transform said host species of bacteria.

Illustrative embodiments are defined in more specific claims. For example:

Claim 2. A method for producing a predetermined protein in a stable form in a transformed host species of bacteria, comprising, providing an *E. coli* plasmid having an operator, a promoter, a

site for the initiation of translation, and at least a substantial portion of the beta-galactosidase gene of the *E. coli* lactose operon, said substantial portion of said beta-galactosidase gene being under the control of said operator, promoter and site for initiation of translation, said substantial portion of said beta-galactosidase gene lacking the normal gene termination signal, and linking a heterologous gene encoding said predetermined protein to said beta-galactosidase gene portion at its distal end, said heterologous gene being in proper orientation and having codons arranged in the same reading frame as the codons of the said beta-galactosidase gene portion so that readthrough can occur from said beta-galactosidase gene portion into said heterologous gene in the same reading frame, said heterologous gene portion further containing sufficient DNA sequences to result in expression of a fused protein having sufficient size so as to confer stability on said predetermined protein when said vector is used to transform said host species of bacteria.
Claim 3. The method of Claim 2 wherein said *E. coli* plasmid comprises the plasmid designated pBGP120.
Although the terms in these claims would be familiar to those of ordinary skill in genetic engineering, they employ a bewildering vocabulary new to those who are not versed in molecular biology. An understanding of the science and technology on which these claims are based is essential before one can analyze and explain whether the claimed invention would have been obvious in light of the prior art.

I. *Background* 1

Proteins are biological molecules of enormous importance. Proteins include enzymes that catalyze biochemical reactions, major structural materials of the animal body, and many hormones. Numerous patents and applications for patents in the field of biotechnology involve specific proteins or methods for making and using proteins. Many valuable proteins occur in nature only in minute quantities, or are difficult to purify from natural sources. Therefore, a goal of many biotechnology projects, including appellants' claimed invention, is to devise methods to synthesize useful quantities of specific proteins by controlling the mechanism by which living cells make proteins.
The basic organization of all proteins is the same. Proteins are large polymeric molecules consisting of chains of smaller building blocks, called *amino acids* , that are linked together covalently. 2 The chemical bonds linking amino acids together are called *peptide* bonds, so proteins are also called *poly*

peptides . 3 It is the exact sequence in which the amino acids are strung together in a polypeptide chain that determines the identity of a protein and its chemical characteristics. 4 Although there are only 20 amino acids, they are strung together in different orders to produce the hundreds of thousands of proteins found in nature.

To make a protein molecule, a cell needs information about the sequence in which the amino acids must be assembled. The cell uses a long polymeric molecule, DNA (deoxyribonucleic acid), to store this information. The subunits of the DNA chain are called *nucleotides* . A nucleotide consists of a nitrogen-containing ring compound (called a *base*) linked to a 5-carbon sugar that has a phosphate group attached. 5 DNA is composed of only four nucleotides. They differ from each other in the base region of the molecule. The four bases of these subunits are adenine, guanine, cytosine, and thymine (abbreviated respectively as A, G, C and T). The sequence of these bases along the DNA molecule specifies which amino acids will be inserted in sequence into the polypeptide chain of a protein.

DNA molecules do not participate directly in the synthesis of proteins. DNA acts as a permanent "blueprint" of all of the genetic information in the cell, and exists mainly in extremely long strands (called *chromosomes*) containing information coding for the sequences of many proteins, most of which are not being synthesized at any particular moment. The region of DNA on the chromosome that codes for the sequence of a single polypeptide is called a *gene* , 6 In order to *express* a gene (the process whereby the information in a gene is used to synthesize new protein), a copy of the gene is first made as a molecule of RNA (ribonucleic acid).

RNA is a molecule that closely resembles DNA. It differs, however in that it contains a different sugar (ribose instead of deoxyribose) and the base thymine (T) of DNA is replaced in RNA by the structurally similar base, uracil (U). Making an RNA copy of DNA is called *transcription* . The transcribed RNA copy contains sequences of A, U, C, and G that carry the same information as the sequence of A, T, C, and G in the DNA. That RNA molecule, called *messenger RNA* , then moves to a location in the cell where proteins are synthesized.

The code whereby a sequence of nucleotides along an RNA molecule is translated into a sequence of amino acids in a protein (i.e., the "genetic code") is based on serially reading groups of three adjacent nucleotides. Each combination of three adjacent nucleotides, called a *codon* ,

specifies a particular amino acid. For example, the codon U-G-G in a messenger RNA molecule specifies that there will be a tryptophan molecule in the corresponding location in the corresponding polypeptide. The four bases A, G, C and U can be combined as triplets in 64 different ways, but there are only 20 amino acids to be coded. Thus, most amino acids are coded for by more than one codon. For example, both U-A-U and U-A-C code for tyrosine, and there are six different codons that code for leucine. There are also three codons that do not code for any amino acid (namely, U-A-A, U-G-A, and U-A-G). Like periods at the end of a sentence, these sequences signal the end of the polypeptide chain, and they are therefore called *stop codons* .

The cellular machinery involved in synthesizing proteins is quite complicated, and centers around large structures called *ribosomes* that bind to the messenger RNA. The ribosomes and associated molecules "read" the information in the messenger RNA molecule, literally shifting along the strand of RNA three nucleotides at a time, adding the amino acid specified by that codon to a growing polypeptide chain that is also attached to the ribosome. When a stop codon is reached, the polypeptide chain is complete and detaches from the ribosome.

The conversion of the information from a sequence of codons in an RNA molecule into the sequence of amino acids in a newly synthesized polypeptide is called *translation* . A messenger RNA molecule is typically reused to make many copies of the same protein. Synthesis of a protein is usually terminated by destroying the messenger RNA. (The information for making more of that protein remains stored in DNA in the chromosomes.)

The translation of messenger RNA begins at a specific sequence of nucleotides that bind the RNA to the ribosome and specify which is the first codon that is to be translated. Translation then proceeds by reading nucleotides, three at a time, until a stop codon is reached. If some error were to occur that shifts the frame in which the nucleotides are read by one or two nucleotides, all of the codons after this shift would be misread. For example, the sequence of codons [. . . *C-U-C-A-G-C-G-U-U-A-C-C-* A. . .] codes for the chain of amino acids [. . .leucine-serine-valine-threonine-. . .]. If the reading of these groups of three nucleotides is displaced by one nucleotide, such as [. . . *C-U-C-A-G-C-G-U-U-A-C-C-A* . . .], the resulting

peptide chain would consist of [. . . serine-alanine-leucine-proline. . .]. This would be an entirely different peptide, and most probably an undesirable and useless one. Synthesis of a particular protein requires that the correct register or *reading frame* be maintained as the codons in the RNA are translated.

The function of messenger RNA is to carry genetic information (transcribed from DNA) to the protein synthetic machinery of a cell where its information is translated into the amino acid sequence of a protein. However, some kinds of RNA have other roles. For example, ribosomes contain several large strands of RNA that serve a structural function (*ribosomal RNA*). Chromosomes contain regions of DNA that code for the nucleotide sequences of structural RNAs and these sequences are transcribed to manufacture those RNAs. The DNA sequences coding for structural RNAs are still called genes even though the nucleotide sequence of the structural RNA is never translated into protein.

Man, other animals, plants, protozoa, and yeast are *eucaryotic* (or eukaryotic) organisms: their DNA is packaged in chromosomes in a special compartment of the cell, the nucleus. Bacteria (*procaryotic* or prokaryotic organisms) have a different organization. Their DNA, usually a circular loop, is not contained in any specialized compartment. Despite the incredible differences between them, all organisms, whether eucaryote or procaryote, whether man or mouse or lowly bacterium, use the same molecular rules to make proteins under the control of genes. In all organisms, codons in DNA are transcribed into codons in RNA which is translated on ribosomes into polypeptides according to the same genetic code. Thus, if a gene from a man is transferred into a bacterium, the bacterium can manufacture the human protein. Since most commercially valuable proteins come from man or other eucaryotes while bacteria are essentially little biochemical factories that can be grown in huge quantities, one strategy for manufacturing a desired protein (for example, insulin) is to transfer the gene coding for the protein from the eucaryotic cell where the gene normally occurs into a bacterium.

Bacteria containing genes from a foreign source (*heterologous* genes) integrated into their own genetic makeup are said to be *transformed* . When transformed bacteria grow and divide, the inserted heterologous genes, like all the other genes that are normally present in the bacterium (*indigenous* genes), are replicated and passed on to succeeding generations. One can produce large quantities of transformed bacteria that contain transplanted heterologous genes. The process of making large quantities of identical copies of a gene (or other fragment of DNA) by introducing it into procaryotic cells and then growing those cells is called *cloning* the gene. After growing

sufficient quantities of the transformed bacteria, the biotechnologist must induce the transformed bacteria to *express* the cloned gene and make useful quantities of the protein. This is the purpose of the claimed invention.

In order to make a selected protein by expressing its cloned gene in bacteria, several technical hurdles must be overcome. First the gene coding for the specific protein must be isolated for cloning. This is a formidable task, but recombinant DNA technology has armed the genetic engineer with a variety of

techniques to accomplish it. 7 Next the isolated gene must be introduced into the host bacterium. This can be done by incorporating the gene into a cloning vector. A *cloning vector* is a piece of DNA that can be introduced into bacteria and will then replicate itself as the bacterial cells grow and divide. Bacteriophage (viruses that infect bacteria) can be used as cloning vectors, but plasmids were the type used by appellants. A *plasmid* is a small circular loop of DNA found in bacteria, separate from the chromosome, that replicates like a chromosome. It is like a tiny auxilliary chromosome containing only a few genes. Because of their small size, plasmids are convenient for the molecular biologist to isolate and work with. Recombinant DNA technology can be used to modify plasmids by splicing in cloned eucaryotic genes and other useful segments of DNA containing control sequences. Short pieces of DNA can even be designed to have desired nucleotide sequences, synthesized chemically, and spliced into the plasmid. One use of such chemically synthesized linkers is to insure that the inserted gene has the same reading frame as the rest of the plasmid; this is a teaching of the Bahl reference cited against appellants. A plasmid constructed by the molecular geneticist can be inserted into bacteria, where it replicates as the bacteria grow.

Even after a cloned heterologous gene has been successfully inserted into bacteria using a plasmid as a cloning vector, and replicates as the bacteria grow, there is no guarantee that the gene will be expressed, i.e., transcribed and translated into protein. A bacterium such as *E. coli* (the species of bacterium used by appellants) has genes for several thousand proteins. At any given moment many of those genes are not expressed at all. The genetic engineer needs a method to "turn on" the cloned gene and force it to be expressed. This is the problem appellants worked to solve.

II. *Prior art*

Appellants sought to control the expression of cloned heterologous genes inserted into bacteria. They reported the results of their early efforts in a publication, the three authors of which included two of the three coinventor-appellants (the Polisky reference 8), that is undisputed prior art against them. Their strategy was to link the foreign gene to a highly regulated indigenous gene. Turning on expression of the indigenous gene by normal control mechanisms of the host would cause expression of the linked heterologous gene.

As a controllable indigenous gene, the researchers chose a gene in the bacterium *E. coli* that makes beta-galactosidase. *Beta-galactosidase* is an enzyme needed to digest the sugar, lactose (milk sugar). When *E. coli* grows in a medium that contains no lactose, it does not make beta-galactosidase. If lactose is added to the medium, the gene coding for beta galactosidase is expressed. The bacterial cell makes beta-galactosidase and is then able to use lactose as a food source. When lactose is no longer available, the cell again stops expressing the gene for beta galactosidase.

The molecular mechanisms through which the presence of lactose turns on expression of the beta-galactosidase gene has been studied in detail, and is one of the best understood examples of how gene expression is regulated on the molecular level. The beta-galactosidase gene is controlled by segments of DNA adjacent to the gene. These *regulatory DNA sequences* (the general term used in Claim 1) include the *operator* and *promoter* sequences (specified in Claim 2). 9 The researchers constructed a plasmid containing the beta-galactosidase gene with its operator and promoter. This gene (with its regulatory sequences) was removed from the chromosome of *E. coli* where it is normally found and was transplanted to a plasmid that could be conveniently manipulated.

Restriction endonucleases are useful tools in genetic engineering. These enzymes cut strands of DNA, but only at places where a specific sequence of nucleotides is present. For example, one restriction endonuclease, called *EcoRI* , cuts DNA only at sites where

the nucleotide sequence is [. . .-G-A-A-T-T-C-. . .]. With restriction enzymes the genetic engineer can cut a strand of DNA at very specific sites into just a few pieces. With the help of

"repair" enzymes, other pieces of DNA can be spliced onto the cut ends. The investigators found that the plasmid which they had constructed contained only two sequences that were cut by EcoRI. They were able to eliminate one of these sites that was unwanted. They were then left with a plasmid containing the beta-galactosidase gene with its regulatory sequences, and a single EcoRI site that was within the beta-galactosidase gene and close to its stop codon. They named this plasmid that they had constructed pBGP120.

The next step was to cut the plasmid open at its EcoRI site and insert a heterologous gene from another organism. The particular heterologous gene they chose to splice in was a segment of DNA from a frog that coded for ribosomal RNA. The frog gene was chosen as a test gene for reasons of convenience and availability. The new plasmid created by inserting the frog gene was similar to pBGP120, but its beta-galactosidase gene was incomplete. Some codons including the stop codon were missing from its end, which instead continued on with the sequence of the frog ribosomal RNA gene. The investigators named this new plasmid pBGP123. They inserted this plasmid back into *E. coli* and grew sufficient quantities for study. They then fed the *E. coli* with lactose. As they had intended, the lactose turned on transcription of the beta-galactosidase gene in the plasmid. RNA polymerase moved along the plasmid producing a strange new kind of RNA: Each long strand of RNA first contained codons for the messenger RNA for beta-galactosidase and then continued without interruption with the codons for the frog ribosomal RNA. Thus, there was *read-through* transcription in which the RNA polymerase first transcribed the indigenous (beta-galactosidase) gene and then "read through," i.e., continued into and through the adjacent heterologous (frog ribosomal RNA) gene. Although the RNA produced was a hybrid, it nevertheless contained a nucleotide sequence dictated by DNA from a frog. The researchers had achieved the first controlled transcription of an animal gene inside a bacterium. The researchers had used a gene coding for a ribosomal RNA as their heterologous test gene. Ribosomal RNA is not normally translated into protein. Nevertheless, they were obviously interested in using their approach to make heterologous proteins in bacteria. They therefore examined the beta-galactosidase made by their transformed bacteria. Patrick O'Farrell, who was not a coauthor of the Polisky paper but was to become a coinventor in the patent application, joined as a collaborator. They found that beta-galactosidase from the transformed bacteria had a higher molecular weight than was normal. They concluded that the bacteria must have used their strange new hybrid RNA like any other messenger RNA and translated it into protein. When the machinery of protein synthesis reached the premature end of the sequence coding for

beta-galactosidase it continued right on, three nucleotides at a time, adding whatever amino acid was coded for by those nucleotides, until a triplet was reached with the sequence of a stop codon. The resulting polypeptide chains had more amino acids than normal beta-galactosidase, and thus a higher molecular weight. The researchers published their preliminary results in the Polisky article. They wrote:

f the normal translational stop signals for [beta]-galactosidase are missing in pBGP120, in-phase translational readthrough into adjacent inserted sequences might occur, resulting in a significant increase in the size of the [beta]-galactosidase polypeptide subunit. In fact, we have recently observed that induced cultures of pBGP123 contain elevated levels of [beta]-galactosidase of higher subunit molecular weight than wild-type enzyme (P. O'Farrell, unpublished experiments). We believe this increase results from translation of *Xenopus* [frog] RNA sequences covalently linked to [messenger] RNA for [beta]-galactosidase, resulting in a fused polypeptide.

Polisky at 3904.

Since ribosomal RNA is never translated in normal cells, the polypeptide chain produced by translating that chain was not a naturally occurring, identified protein. The authors of the Polisky paper explicitly pointed out that if one were to insert a heterologous gene coding for a protein into their plasmid, it should produce a "fused protein" consisting of a polypeptide made of beta-galactosidase plus the protein coded for by the inserted gene, joined by a peptide bond into a single continuous polypeptide chain:

It would be interesting to examine the expression of a normally translated eukaryotic sequence in pBGP120. If an inserted sequence contains a ribosome binding site that can be utilized in bacteria, production of high levels of a readthrough transcript might allow for extensive translation of a functional eukaryotic polypeptide. In the absence of an independent ribosome bind

ing site, the eukaryotic sequence would be translated to yield a peptide covalently linked to [beta]-galactosidase. The extent of readthrough translation under *lac* control will depend on the number of translatable codons between the EcoRI site and the first in-phase nonsense [i.e., stop] codon in the inserted sequence.

Id.

III. *The Claimed Invention*

Referring back to Claims 1 through 3, it can be seen that virtually everything in the claims was present in the prior art Polisky article. The main difference is that in Polisky the heterologous gene was a gene for ribosomal RNA while the claimed invention substitutes a gene coding for a predetermined protein. Ribosomal RNA gene is not normally translated into protein, so expression of the heterologous gene was studied mainly in terms of transcription into RNA. Nevertheless, Polisky mentioned preliminary evidence that the transcript of the ribosomal RNA gene was translated into protein. Polisky further predicted that if a gene that codes for a protein were to be substituted for the ribosomal RNA gene, "a readthrough transcript might allow for extensive translation of a functional eukaryotic polypeptide." Thus, the prior art explicitly suggested the substitution that is the difference between the claimed invention and the prior art, and presented preliminary evidence suggesting that the method could be used to make proteins. Appellants reduced their invention to practice some time in 1976 and reported their results in a paper that was published in 1978. 10 During 1977 they communicated their results to another group of researchers who used the readthrough translation approach to achieve the first synthesis of a human protein in bacteria. 11 Appellants filed an application to patent their invention on August 9, 1978, of which the application on appeal is a division.

IV. *The Obviousness Rejection*

The application was rejected under 35 USC 103. The position of the examiner and the Board is, simply, that so much of the appellant's method was revealed in the Polisky reference that making a protein by substituting its gene for the ribosomal RNA gene in Polisky (as suggested by Polisky) would have been obvious to one of ordinary skill in the art at the time that the invention was made.

The claims specify that the heterologous gene should be inserted into the plasmid in the same orientation and with the same reading frame as the preceding portion of the indigenous gene. In view of this limitation, the §103 rejection was based either on Polisky alone (supplemented by the fact that the importance of orientation and reading frame was well known in the prior art) or in combination with the Bahl reference which describes a general method for inserting a piece of chemically synthesized DNA into a plasmid. Bahl teaches that this technique could be used to shift the sequence of DNA inserted into a plasmid into the proper reading frame.

Appellants argue that at the time the Polisky article was published, there was significant unpredictability in the field of molecular biology so that the Polisky article would not have rendered the claimed method obvious to one of ordinary skill in the art. Even though there was speculation in the article that genes coding for proteins could be substituted for the ribosomal RNA gene and would be expressed as readthrough translation into the protein, this had never been done. Appellants say that it was not yet certain whether a heterologous protein could actually be produced in bacteria, and if it could, whether additional mechanisms or methods would be required. They contend

that without such certainty the predictions in the Polisky paper, which hindsight now shows to have been correct, were merely invitations to those skilled in the art to try to make the claimed invention. They argue that the rejection amounts to the application of a standard of "obvious to try" to the field of molecular biology, a standard which this court and its predecessors have repeatedly rejected as improper grounds for a §103 rejection. *E.g., In re Fine* , 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1599 (Fed. Cir. 1988); *In re Geiger* , 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); *In re Merck & Co., Inc* ., 800 F.2d 1091, 1097, 231 USPQ 375, 379 (Fed. Cir. 1986); *In re Antonie* , 559 F.2d 618, 620, 195 USPQ 6, 8 (CCPA 1977). Obviousness under §103 is a question of law. *Panduit Corp. v. Dennison Mfg. Co* ., 810 F.2d 1561, 1568, 1 USPQ2d 1593, 1597 (Fed. Cir.), *cert. denied* , 107 S.Ct. 2187 (1987). An analysis of obviousness must be based on several factual inquiries: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and (4) objective evidence of nonobviousness, if any. *Graham v. John Deere Co* ., 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966). *See, e.g* ., *Custom Accessories, Inc. v. Jeffrey-Allan Indus* ., 807 F.2d 955, 958, 1 USPQ2d 1196, 1197 (Fed. Cir. 1986). The scope and content of the prior art and the differences between the prior art and the claimed invention have been examined in sections II and III, *supra* . Appellants say that in 1976 those of ordinary skill in the arts of molecular biology and recombinant DNA technology were research scientists who had "extraordinary skill in relevant arts" and "were among the brightest biologists in the world." Objective evidence of nonobviousness was not argued.

[1] With the statutory factors as expounded by *Graham* in mind and considering all of the evidence, this court must determine the correctness of the board's legal determination that the claimed invention as a whole would have been obvious to a person having ordinary skill in the art at the time the invention was made. We agree with the board that appellants' claimed invention would have been obvious in light of the Polisky reference alone or in combination with Bahl within the meaning of §103. Polisky contained detailed enabling methodology for practicing the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful.

[2] Appellants argue that after the publication of Polisky, successful synthesis of protein was still uncertain. They belittle the predictive value of the observation that expression of the transcribed RNA in Polisky produced beta-galactosidase with a greater than normal molecular weight, arguing that since ribosomal RNA is not normally translated, the polypeptide chains that were added to the end of the beta-galactosidase were "junk" or "nonsense" proteins. This characterization ignores the clear implications of the reported observations. The Polisky study directly proved that a readthrough transcript messenger RNA had been produced. The preliminary observation showed that this messenger RNA was read and used for successful translation. It was well known in the art that ribosomal RNA was made of the same nucleotides as messenger RNA, that any sequence of nucleotides could be read in groups of three as codons, and that reading these codons should specify a polypeptide chain that would elongate until a stop codon was encountered. The preliminary observations thus showed that codons beyond the end of the beta-galactosidase gene were being translated into peptide chains. This would reasonably suggest to one skilled in the art that if the codons inserted beyond the end of the beta-galactosidase gene coded for a "predetermined protein," that protein would be produced. In other words, it would have been obvious and reasonable to conclude from the observation reported in Polisky that since nonsense RNA produced nonsense polypeptides, if meaningful RNA was inserted instead of ribosomal RNA, useful protein would be the result. The relative shortness of the added chains is also not a source of uncertainty, since one skilled in the art would have known that a random sequence of nucleotides would produce a stop codon before the chain got too long. 12

Appellants complain that since predetermined proteins had not yet been produced in transformed bacteria, there was uncertainty as to whether this could be done, and that the rejection is thus founded on an impermissible "obvious to try" standard. It is true that this court and its

predecessors have repeatedly emphasized that "obvious to try" is not the standard under §103. However, the meaning of this maxim is sometime lost. Any invention that would in fact have been obvious under §103 would also have been, in a sense, obvious to try. The question is: when is an

invention that was obvious to try nevertheless nonobvious?

[3] The admonition that "obvious to try" is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. *E.g .*, *In re Geiger* , 815 F.2d at 688, 2 USPQ2d at 1278; *Novo Industri A/S v. Travenol Laboratories, Inc .*, 677 F.2d 1202, 1208, 215 USPQ 412, 417 (7th Cir. 1982); *In re Yates* , 663 F.2d 1054, 1057, 211 USPQ 1149, 1151 (CCPA 1981); *In re Antonie* , 559 F.2d at 621, 195 USPQ at 8-9. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. *In re Dow Chemical Co .*, 837 F.2d, 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1985); *Hybritech, Inc. v. Monoclonal Antibodies, Inc .*, 802 F.2d 1367, 1380, 231 USPQ 81, 90-91 (Fed. Cir. 1 986), *cert. denied* , 107 S.Ct. 1606 (1987); *In re Tomlinson* ; 363 F.2d 928, 931, 150 USPQ 623, 626 (CCPA 1966). Neither of these situations applies here.

[4] Obviousness does not require absolute predictability of success. Indeed, for many inventions that seem quite obvious, there is no absolute predictability of success until the invention is reduced to practice. There is always at least a possibility of unexpected results, that would then provide an objective basis for showing that the invention, although apparently obvious, was in law nonobvious. *In re Merck & Co .*, 800 F.2d at 1098, 231 USPQ at 380; *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co .*, 730 F.2d 1452, 1461, 221 USPQ 481, 488 (Fed. Cir. 1984); *In re Papesch* , 315 F.2d 381, 386-87, 137 USPQ 43, 47-48 (CCPA 1963). For obviousness under §103, all that is required is a reasonable expectation of success. *In re Longi* , 759 F.2d 887, 897, 225 USPQ 645, 651-52 (Fed. Cir. 1985); *In re Clinton* , 527 F.2d

1226, 1228, 188 USPQ 365, 367 (CCPA 1976). The information in the Polisky reference, when combined with the Bahl reference provided such a reasonable expectation of success. Appellants published their pioneering studies of the expression of frog ribosomal RNA genes in bacteria more than a year before they applied for a patent. After providing virtually all of their method to the public without applying for a patent within a year, they foreclosed themselves from obtaining a patent on a method that would have been obvious from their publication to those of ordinary skill in the art, with or without the disclosures of other prior art. The decision of the board is

AFFIRMED .

Footnotes

Footnote 1. Basic background information about molecular biology and genetic engineering, can be found in Alberts, Bray, Lewis, Raff, Roberts & Watson, *The Molecular Biology of the Cell* , 1-253, 385-481 (1983) [hereinafter *The Cell*]; Watson, Hopkins, Roberts, Steitz & Weiner, *The Molecular Biology of the Gene* , Vol. 1 (4th ed., 1987) 3-502 [hereinafter *The Gene*]. These standard textbooks were used to supplement the information in the glossary supplied by appellants. The description here is necessarily simplified and omits important facts and concepts that are not necessary for the analysis of this case.

Footnote 2. There are twenty amino acids: alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan, glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine, aspartic acid, glutamic acid, lysine, arginine, and histidine.

Footnote 3. Proteins are often loosely called *peptides* , but technically proteins are only the larger peptides with chains of at least 50 amino acids, and more typically hundreds of amino acids. Some proteins consist of several polypeptide chains bound together covalently or noncovalently. The term "peptide" is broader than "protein" and also includes small chains of amino acids linked by peptide bonds, some as small as two amino acids. Certain small peptides

have commercial or medical significance.

Footnote 4. Polypeptide chains fold up into complex 3-dimensional shapes. It is the shape that actually determines many chemical properties of the protein. However, the configuration of a protein molecule is determined by its amino acid sequence. *The Cell* at 111-12; *The Gene* at 50-54.

Footnote 5. The sugar in DNA is deoxyribose, while the sugar in RNA, *infra* , is ribose. The sugar and phosphate groups are linked covalently to those of adjacent nucleotides to form the backbone of the long unbranched DNA molecule. The bases project from the chain, and serve as the "alphabet" of the genetic code.

DNA molecules actually consist of two chains tightly entwined as a double helix. The chains are not identical but instead are complementary: each A on one chain is paired with a T on the other chain, and each C has a corresponding G. The chains are held together by noncovalent bonds between these complementary bases. This double helical structure plays an essential role in the replication of DNA and the transmission of genetic information. *See generally The Cell* at 98-106; *The Gene* at 65-79. However, the information of only one strand is used for directing protein synthesis, and it is not necessary to discuss the implication of the double-stranded structure of DNA here. RNA molecules, *infra* , are single stranded.

Footnote 6. Chromosomes also contain regions of DNA that are not part of genes, i.e., do not code for the sequence of amino acids in proteins. These include sections of DNA adjacent to genes that are involved in the control of transcription, *infra* , and regions of unknown function.

Footnote 7. See *The Cell* at 185-194; *The Gene* at 208-10.

Footnote 8. Polisky, Bishop & Gelfand, *A plasmid cloning vehicle allowing regulated expression of eukaryotic DNA in bacteria* , 73 Proc. Nat'l Acad. Sci. USA 3900 (1976).

Footnote 9. The *promoter* is a sequence of nucleotides where the enzyme that synthesizes RNA, *RNA polymerase* , attaches to the DNA to start the transcription of the beta-galactosidase gene. The *operator* is an overlapping DNA sequence that binds a small protein present in the cell, the lactose repressor protein. The lactose repressor protein binds to the operator and physically blocks the RNA polymerase from properly attaching to the promoter so that transcription cannot proceed. Lactose molecules interact with the lactose repressor protein and cause it to change its shape; after this change in shape it moves out of the way and no longer prevents the RNA polymerase from binding to the promoter. Messenger RNA coding for beta-galactosidase can then be transcribed. *See generally The Cell* at 438-39; *The Gene* at 474-80.

Footnote 10. O'Farrell, Polisk & Gelfand, *Regulated expression by readthrough translation from a plasmid-encoded beta-galactosidase* , 134 J. Bacteriol. 645 (1978). The heterologous genes expressed in these studies were not predetermined, but were instead unidentified genes of unknown origin. The authors speculated that they were probably genes from *E. coli* that were contaminants in the source of beta-galactosidase genes. *Id* . at 648

Footnote 11. Itakura, Hirose, Crea, Riggs, Heynecker, Bolivar & Boyer, *Expression in Escherichia coli of a chemically synthesized gene for the hormone samatostatin* , 198 Science 1056 (1977). A pioneering accomplishment of the Itakura group is that the gene was not from a human source, but instead was entirely synthesized in the laboratory using chemical methods. It is not clear whether the appellants communicated only the results reported in the Polisky publication or whether they communicated the complete claimed invention.

Footnote 12. The patent application indicates that chains as long as 60 amino acids were added, which is hardly a trivial length of polypeptide.

- End of Case -

In re Fine

U.S. Court of Appeals Federal Circuit
5 USPQ2d 1596

Decided January 26, 1988
No. 87-1319

Headnotes

PATENTS

1. Patentability/Validity -- Obviousness -- Evidence of (§ 115.0903)

Patent and Trademark Office improperly rejected claimed invention for obviousness since nothing in cited references, either alone or in combination, suggests or teaches claimed invention, since there is consequently no support for PTO's conclusion that substitution of one type of detector for another in prior art system, resulting in claimed invention, would have been obvious, and since PTO therefore failed to satisfy its burden of establishing prima facie case of

obviousness by showing some objective teaching or generally available knowledge that would lead one skilled in art to combine teachings of existing references.

2. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Obviousness is tested by what combined teachings of prior art references would have suggested to those of ordinary skill in art, not by whether particular combination of elements from such references might have been "obvious to try."

3. Patentability/Validity -- Obviousness -- Evidence of (§ 115.0903)

Patent and Trademark Office erred, in rejecting as obvious system for detecting and measuring minute quantities of nitrogen compounds, by failing to recognize that appealed claims can be distinguished over combination of prior art references, in view of evidence demonstrating that prior art does not teach claimed temperature range, despite some overlap of preferred temperature ranges for claimed invention and prior art, since purposes of preferred temperature ranges are different and overlap is mere happenstance.

4. Patentability/Validity -- Obviousness -- In general (§ 115.0901)

Dependent claims are non-obvious under 35 USC 103 if claims from which they depend are non-obvious.

Case History and Disposition:

Appeal from the U.S. Patent and Trademark Office Board of Patent Appeals and Interferences.

Application for patent by David H. Fine, Serial No. 512,374. From decision of Board of Patent Appeals and Interferences affirming rejection of application, applicant appeals. Reversed; Smith, circuit judge, dissenting with opinion.

Attorneys:

Morris Relson and Darby & Darby, New York, N.Y., (Beverly B. Goodwin with them on the brief) for appellant.

Lee E. Barrett, associate solicitor, Arlington, Va., (Joseph F. Nakamura, solicitor, and Fred E. McKelvey, deputy solicitor, with him on the brief) for appellee.

Judge:

Before Friedman, Smith, and Mayer, circuit judges.

Opinion Text

Opinion By:

Mayer, J.

David H. Fine appeals from a decision of the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office (Board) affirming the rejection of certain claims of his application, Serial No. 512,374, and concluding that his invention would have been obvious to one of ordinary skill in the art and was therefore unpatentable under 35 U.S.C. §103. We reverse.

Background

A. *The Invention .*

The invention claimed is a system for detecting and measuring minute quantities of nitrogen compounds. According to Fine, the system has the ability to detect the presence of nitrogen compounds in quantities as minute as one part in one billion, and is an effective means to detect drugs and explosives, which emanate nitrogen compound vapors even when they are concealed in luggage and closed containers.

The claimed invention has three major components: (1) a gas chromatograph which separates a gaseous sample into its constituent parts; (2) a converter which converts the nitrogen compound effluent output of the chromatograph into nitric oxide in a hot, oxygen-rich environment; and (3) a detector for measuring the level of nitric oxide. The claimed invention's sensitivity is achieved by combining nitric oxide with ozone to produce nitrogen dioxide which concurrently causes a detectable luminescence. The luminescence, which is measured by a visual detector, shows the level of nitric oxide which in turn is a measure of nitrogen compounds found in the sample.

The appealed claims were rejected by the Patent and Trademark Office (PTO) under 35 U.S.C. §103. Claims 60, 63, 77 and 80 were rejected as unpatentable over Eads, Patent No. 3,650,696 (Eads) in view of Warnick, et al., Patent No. 3,746,513 (Warnick). Claims 62, 68, 69, 79, 85 and 86 were rejected as unpatentable over Eads and Warnick in view of Glass, et al., Patent No. 3,207,585 (Glass).

B. *The Prior Art .*

1. *Eads Patent .*

Eads discloses a method for separating, identifying and quantitatively monitoring sulfur compounds. The Eads system is used primarily in "air pollution control work in the scientific characterization of odors from sulfur compounds."

The problem addressed by Eads is the tendency of sulfur compounds "to adhere to or react with the surface materials of the sampling and analytical equipment, and/or react with the liquid or gaseous materials in the equipment." Because of this, the accura

cy of measurement is impaired. To solve the problem, the Eads system collects an air sample containing sulfur compounds in a sulfur-free methanol solution. The liquid is inserted into a gas chromatograph which separates the various sulfur compounds. The compounds are next sent through a pyrolysis furnace where they are oxidized to form sulfur dioxide. Finally, the sulfur dioxide passes through a measuring device called a microcoulometer which uses titration cells to calculate the concentration of sulfur compounds in the sample.

2. *Warnick Patent*.

Warnick is directed to a means for detecting the quantity of pollutants in the atmosphere. By measuring the chemiluminescence of the reaction between nitric oxide and ozone, the Warnick device can detect the concentration of nitric oxide in a sample gaseous mixture.
Warnick calls for "continuously flowing" a sample gaseous mixture and a reactant containing ozone into a reaction chamber. The chemiluminescence from the resulting reaction is transmitted through a light-transmitting element to produce continuous readouts of the total amount of nitric oxide present in the sample.

3. Glass Patent.

The invention disclosed in Glass is a device for "completely burning a measured amount of a substance and analyzing the combustion products." A fixed amount of a liquid petroleum sample and oxygen are supplied to a flame. The flame is then spark-ignited, causing the sample to burn. The resulting combustion products are then collected and measured, and from this measurement the hydrogen concentration in the sample is computed.

C. *The Rejection*.

The Examiner rejected claims 60, 63, 77 and 80 because "substitution of the [nitric oxide] detector of Warnick for the sulfur detector of Eads would be an obvious consideration if interested in nitrogen compounds, and would yield the claimed invention." He further asserted that "Eads teaches the [claimed] combination of chromatograph, combustion, and detection, in that order. . . . Substitution of detectors to measure any component of interest is well within the skill of the art." In rejecting claims 62, 68, 69, 79, 85 and 86, the Examiner said, "Glass et al.

teach a flame conversion means followed by a detector, and substitution of the flame conversion means of Glass et al. for the furnace of Eads would be an obvious equivalent and would yield the claimed invention." The Board affirmed the Examiner's rejection.

Discussion

A. *Standard of Review .*

Obviousness under 35 U.S.C. §103 is " 'a legal conclusion based on factual evidence.' " *Stratoflex, Inc. v. Aeroquip Corp* ., 713 F.2d 1530, F.2d 1530, 1535, 218 USPQ 871, 876 (Fed. Cir. 1983) (quoting *Stevenson v. Int'l Trade Comm'n* , 612 F.2d 546, 549, 204 USPQ 276, 279 (CCPA 1979)). Therefore, an obviousness determination is not reviewed under the clearly erroneous standard applicable to fact findings, *Raytheon Co. v. Roper Corp* ., 724 F.2d 951, 956, 220 USPQ 592, 596 (Fed. Cir. 1983); it is "reviewed for correctness or error as a matter of law." *In re De Blauwe* , 736 F.2d 699, 703, 222 USPQ 191, 195 (Fed. Cir. 1984).
To reach a proper conclusion under §103, the decisionmaker must step backward in time and into the shoes worn by [a person having ordinary skill in the art] when the invention was unknown and just before it was made. In light of *all* the evidence, the decisionmaker must then determine whether . . . the claimed invention as a whole would have been obvious at *that* time to *that* person. 35 U.S.C. §103. The answer to that question partakes more of the nature of law than of fact, for it is an ultimate conclusion based on a foundation formed of all the probative facts. *Panduit Corp. v. Dennison Mfg. Co* ., 810 F.2d 1561, 1566, 1 USPQ2d 1593, 1595-96 (Fed. Cir. 1987).

B. *Prima Facie Obviousness .*

Fine says the PTO has not established a *prima facie* case of obviousness. He contends the references applied by the Board and Examiner were improperly combined, using hindsight reconstruction, without evidence to support the combination and in the face of contrary teachings in the prior art. He argues that the appealed claims were rejected because the PTO thought it would have been "obvious to try" the claimed invention, an unacceptable basis for rejection.
[1] We agree. The PTO has the burden under section 103 to establish a *prima facie* case of obviousness. *See In re Piasecki* , 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-87 (Fed. Cir. 1984). It can satisfy this burden only by showing some objective teaching in the prior art or that

knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. *In re Lalu* , 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984); *see also Ashland Oil, Inc. v. Delta Resins & Refractories, Inc* .,

776 F.2d 281, 297 n.24, 227 USPQ 657 , 667 n.24 (Fed. Cir. 1985); *ACS Hosp. Sys., Inc. v. Montefiore Hosp* ., 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). This it has not done. The Board points to nothing in the cited references, either alone or in combination, suggesting or teaching Fine's invention.

The primary basis for the Board's affirmance of the Examiner's rejection was that it would have been obvious to substitute the Warnick nitric oxide detector for the Eads sulfur dioxide detector in the Eads system. The Board reiterated the Examiner's bald assertion that "substitution of one type of detector for another in the system of Eads would have been within the skill of the art," but neither of them offered any support for or explanation of this conclusion.

Eads is limited to the analysis of sulfur compounds. The particular problem addressed there is the difficulty of obtaining precise measurements of sulfur compounds because of the tendency of sulfur dioxide to adhere to or react with the sampling analytic equipment or the liquid or gaseous materials in the equipment. It solves this problem by suggesting that the gaseous sample containing sulfur compounds be absorbed into sulfur-free methanol and then inserted into a gas chromatograph to separate the sulfur compounds.

There is no suggestion in Eads, which focuses on the unique difficulties inherent in the measurement of sulfur, to use that arrangement to detect nitrogen compounds. In fact, Eads says that the presence of nitrogen is undesirable because the concentration of the titration cell components in the sulfur detector is adversely affected by substantial amounts of nitrogen compounds in the sample. So, instead of suggesting that the system be used to detect nitrogen compounds, Eads deliberately seeks to avoid them; it warns against rather than teaches Fine's invention. *See W. L. Gore & Assoc. v. Garlock, Inc* ., 721 F.2d 1540, 1550, 220 USPQ 303, 311 (Fed. Cir. 1983) (error to find obviousness where references "diverge from and teach away from the invention at hand"). In the face of this, one skilled in the art would not be expected to combine a nitrogen-related detector with the Eads system. Accordingly, there is no suggestion to combine Eads and Warnick.

Likewise, the teachings of Warnick are inconsistent with the claimed invention, to some extent. The Warnick claims are directed to a gas stream from engine exhaust "continuously flowing the gaseous mixtures into the reaction chamber" to obtain "continuous readouts" of the amount of nitric oxide in the sample. The other words, it contemplates measuring the total amount of nitric oxide in a continuously flowing gaseous mixture of unseparated nitrogen constituents. By contrast, in Fine each nitrogen compound constituent of the gaseous sample is retained in the Chromatograph for an individual time period so that each exists in discrete, time-separated pulses. * By this process, each constituent may be both identified by its position in time sequence, and measured. The claimed system, therefore, diverges from Warnick and teaches advantages not appreciated or contemplated by it.

Because neither Warnick nor Eads, alone or in combination, suggests the claimed invention, the Board erred in affirming the Examiner's conclusion that it would have been obvious to substitute the Warnick nitric oxide detector for the Eads sulfur dioxide detector in the Eads system. *ACS Hosp. Sys* ., 732 F.2d at 1575-77, 221 USPQ at 931-33. The Eads and Warnick references disclose, at most, that one skilled in the art might find it obvious to try the claimed invention. But whether a particular combination might be "obvious to try" is not a legitimate test of patentability. *In re Geiger* , 815 F.2d 868, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); *In re Goodwin* , 576 F.2d 375, 377, 198 USPQ 1, 3 (CCPA 1978).

[2] Obviousness is tested by "what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re Keller* , 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). But it "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." *ACS Hosp. Sys* ., 732 F.2d at 1577, 221 USPQ at 933. And "teachings of references can be combined *only* if there is some suggestion or incentive to do so." *Id* . Here, the prior art contains none.

Instead, the Examiner relies on hindsight in reaching his obviousness determination.

But this court has said, "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which

only the inventor taught is used against its teacher." *W. L. Gore* , 721 F.2d at 1553, 220 USPQ at 312-13. It is essential that "the decisionmaker forget what he or she has been taught at trial about the claimed invention and cast the mind back to the time the invention was made . . . to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art." *Id* . One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

C. *Advantage Not Appreciated by the Prior Art* .

[3] The Board erred not only in improperly combining the Eads and Warnick references but also in failing to appreciate that the appealed claims can be distinguished over that combination. A material limitation of the claimed system is that the conversion to nitric oxide occur in the range of 600°C to 1700°C. The purpose of this limitation is to prevent nitrogen from other sources, such as the air, from being converted to nitric oxide and thereby distorting the measurement of nitric oxide derived from the nitrogen compounds of the sample.

The claimed nitric oxide conversion temperature is not disclosed in Warnick. Although Eads describes a preferred temperature of 675°C to 725°C, the purpose of this range is different from that of Fine. Eads requires the 675°C to 725°C range because it affords a temperature low enough to avoid formation of unwanted sulfur trioxide, yet high enough to avoid formation of unwanted sulfides. Fine's temperature range, in contrast, does not seek to avoid the formation of sulfur compounds or even nitrogen compounds. It enables the system to break down the nitrogen compounds of the sample while avoiding the destruction of background nitrogen gas. There is a partial overlap, of course, but this is mere happenstance. Because the purposes of the two temperature ranges are entirely unrelated, Eads does not teach use of the claimed range. *See In re Geiger* , 815 F.2d at 688, 2 USPQ2d at 1278. The Board erred by concluding otherwise.

D. *Unexpected Results* .

Because we reverse for failure to establish a *prima facie* case of obviousness, we need not reach Fine's contention that the Board failed to accord proper weight to the objective evidence of unexpected superior results. *Id* .

E. *The "Flame" Claims* .

[4] Claims 62, 68, 69, 79, 85 and 86 relate to the oxygen-rich flame conversion means of the claimed invention. These "flame" claims depend from either apparatus claim 60 or method claim 77. Dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious. *Hartness Int'l, Inc. v. Simplimatic Eng'g Co* ., 819 F.2d 1100, 1108, 2 USPQ2d 1826, 1831 (Fed. Cir. 1987); *In re Abele* , 684 F.2d 902, 910, 214 USPQ 682, 689 (CCPA 1982); *see also In re Sernaker* , 702 F.2d 989, 991, 217 USPQ 1, 3 (Fed. Cir. 1983). In view of our conclusion that claims 60 and 77 are nonobvious, the dependent "flame" claims are also patentable.

Conclusion

The Board's decision affirming the Examiner's rejection of claims 60, 62, 63, 68, 69, 77, 79, 80, 85 and 86 of Fine's application as unpatentable over the prior art under 35 U.S.C. §103 is *REVERSED* .

Footnotes

Footnote *. The Solicitor argues that the contents of Attachment C of Fine's brief were not before the Board and may not properly be considered here. However, we need not rely on Attachment C. It is merely illustrative of the qualitative separation of nitrogen compounds which occurs in Fine's system. The fact that the various constituents exit at discrete intervals is shown by the specification which was before the Board and which may appropriately be considered on appeal. *See, e.g., Astra-Sjuco, A.B. v. United States Int'l Trade Comm'n* , 629 F.2d 682, 686, 207 USPQ 1, 5 (CCPA 1980) (claims must be construed in light of specification).

Dissenting Opinion Text

Dissent By:

Smith, circuit judge, dissenting.

I respectfully dissent. I am of the firm belief that the prior art references, relied upon by the PTO

to establish its prima facie case of obviousness, in combination teach and suggest Fine's invention to one skilled in the art. Also, I firmly believe that Fine failed to rebut the PTO's prima facie case. On this basis, I would affirm the board's determination sustaining the examiner's rejection, pursuant to 35 U.S.C. §103, of Fine's claims on appeal before this court.

- End of Case -

In re Lalu and Foulletier

U.S. Court of Appeals Federal Circuit
223 USPQ 1257

Decided Nov. 2, 1984
No. 83-1358

Headnotes

JUDICIAL PRACTICES AND PROCEDURES

1. Patentability/Validity -- Obviousness -- Relevant prior art -- Particular inventions (§ 115.0903.03)

Mere fact that reference cites compounds, structurally similar to applicants' claimed compounds, that can be used as intermediates in production of reference's claimed compounds does not provide adequate motivation for one of ordinary skill in art to stop reference's synthesis and investigate intermediate compounds with expectation of arriving at applicants' claimed

compounds that have different uses, rendering structural obviousness rejection unsupported.

Particular patents - Sulfonic Acids

Lalu and Foulletier, New Polyfluorinated Sulfonic Acids and their Derivatives, rejection of claims 13-22 reversed.

Case History and Disposition:

Appeal from Patent and Trademark Office Board of Appeals.

Application for patent of Jean Pierre Lalu, and Louis Foulletier, Serial No. 966,508, filed Dec. 4, 1978. From decision rejecting claims 13-22, applicants appeal. Reversed.

Attorneys:

Brian Poissant, New York, N.Y. (Clyde C. Metzger, New York, N.Y., of counsel) for appellant.

Joseph F. Nakamura, Solicitor, Jere W. Sears, Deputy Solicitor, and Henry W. Tarring, II, Associate Solicitor, for Patent and Trademark Office.

Judge:

Before Baldwin and Kashiwa, Circuit Judges, and Cowen, Senior Circuit Judge.

Opinion Text

Opinion By:

Baldwin, Circuit Judge.

This appeal is from a decision of the United States Patent and Trademark Office Board of Appeals (board) affirming the rejection under 35 U.S.C. §103 of claims 13-22, all of the claims of appellants' application Serial No. 966,508, filed December 4, 1978, for "New Polyfluorinated Sulphonic Acids and Their Derivatives." We reverse.

The Invention

The invention relates to perfluoroalkyl sulfonyl chlorides and bromides having the formula:

$C_nF_{2n+1}(CH_2)_bSO_2Z$

wherein the perfluoroalkyl group

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

is defined by n being a number between 1 and 20, Z is a chlorine or bromine atom, and the bridging group $(CH_2)_b$ is defined by b being a number between 2 and 20.

The claimed compounds are useful in the textile, leather, and paper industries. The compounds have utility as corrosion inhibiting agents, surface active agents, and leveling agents, and therefore can be incorporated into waxes, greases, varnishes, and paints to improve the spreading out and leveling of such viscous products.

Claim 13, the only independent claim on appeal, is illustrative:

13. A product having the formula

$C_nF_{2n+1}(CH_2)_bSO_2Z$ wherein

C_nF_{2n+1} represents a straight or branched perfluorinated hydrocarbon chain, n is a number between 1 and 20, b is a number between 2 and 20 and Z is a chlorine or bromine atom.

Claims 14-22 depend from claim 13 and further limit the parameters n, b, and Z which define the length of the perfluoroalkyl group, the length of the bridging group, and the nature of the Z halide group, i.e., a chlorine or bromine atom.

The Prior Art

The sole reference relied upon by the board is United States Patent No. 3,130,221 issued April 21, 1964 to Oesterling. Oesterling discloses 1,1-dihydroperfluoroalkyl sulfonic acids having the formula:

$C_nF_{2n+1}CH_2SO_3H$

wherein

$C_nF_{2n+1}(CH_2)_bSO_2Z$ is a lower perfluoroalkyl group and the bridging group is a methylene (CH_2) group. According to Oesterling, "The compounds of this invention include the 1,1-dihydroperfluoroalkyl acids containing from two to five carbon atoms; i.e., from one to four carbon atoms in the * * * [perfluoroalkyl] portion of the molecule." These compounds are strong acids and are used in reactions such as base neutralization, alkylation catalysis, and metal cleaning. Additionally, the compounds are useful as high energy fuels such as liquid rocket propellants because of their relatively high thermal stability. Of the group of acids disclosed by Oesterling, "the preferred compound for use as a high energy fuel is 1,1-dihydroperfluoroethylsulfonic acid [$CF_3CH_2SO_3H$]. As the number of carbon

atoms in the molecule increases, the thermal stability decreases and compounds containing above five carbon atoms are of little value as a fuel."

The claimed sulfonic acids are prepared in the reference by chlorination of the corresponding bis (1,1-dihydroperfluoroalkyl) disulfides to form the corresponding 1,1-dihydroperfluoroalkyl sulfonyl chlorides, which are then hydrolyzed to produce the product 1,1-dihydroperfluoroalkyl sulfonic acids. The intermediate sulfonyl chlorides which are used to prepare the final product acids have the formula:

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

wherein

C_nF_{2n+1} is also a lower perfluoroalkyl group and the bridging group is a methylene (CH_2)

group. Oesterling teaches that the hydrolysis may be carried out without isolation of the intermediate sulfonyl chloride, but it is preferable to hydrolyze isolated sulfonyl chloride in order to obtain a purer sulfonic acid product.

The Rejection

The examiner rejected the claims based on structural obviousness because Oesterling teaches homologous compounds. The examiner said, "Oesterling discloses only one method of preparing the sulfonic acids which *requires* the use of the halide intermediate. One motivated to prepare the homologous acids would similarly be motivated to prepare the homologous acids halides." (emphasis in original).

The board, in affirming the examiner's rejection, said the close structural similarity between the reference sulfonyl chloride compounds and the claimed compounds was sufficient to raise the presumption of obviousness. The board said further:

The fact that the reference teaches that the sulfonyl chloride compounds are useful as an intermediate or a starting compound for the production of a corresponding sulfonic acid as opposed to the appellants' disclosure that the claimed compounds have other utilities does not by itself rebut the prima facie case of obviousness made out by the Examiner. * * *

The case of In re Stemniski, 58 CCPA 1410, 444 F.2d 581, 170 USPQ 343 (1971), is distinguishable since here Oesterling discloses a utility (a starting material for making an acid) for the pertinent sulfonyl chlorides, whereas in Stemniski the reference disclosed no utility for the relevant compound. In view of the unequivocal identification and isolation of the sulfonyl chloride by Oesterling and the specific utility taught for the compound, a starting material for the preparation of a useful acid, the portions of the court's decision in In re Gyurik, 596 F.2d 1012; 201 USPQ 552 (CCPA 1979), relied upon by the appellants are not considered to dictate reversal of the Examiner's holding.

Opinion

Apellants argue that the acid taught by Oesterling is limited to a maximum of five carbon atoms and, therefore, there would be no motivation for one of ordinary skill to prepare an acid, or its predecessor sulfonyl chloride containing more than five carbon atoms. Accordingly, appellants contend that since their compounds may contain up to forty carbon atoms, they are not structurally similar to the Oesterling intermediate sulfonyl chlorides. We disagree with

appellants' contentions because the Oesterling teachings regarding the five carbon atom limitation are related only to the use of the product acid as a high energy fuel. Oesterling discloses other uses for the disclosed sulfonic acids, such as in base neutralization, alkylation catalysis, and metal cleaning, to which the teachings of a five carbon atom limitation do not necessarily apply. Moreover, even if the compounds disclosed by Oesterling are limited to compounds containing two to five carbon atoms, the appellants' compounds contain as few as three carbon atoms.

We are, however, persuaded that the board erred in its conclusion of prima facie obviousness. In determining whether a case of prima facie obviousness exists, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the claimed substitution or other modification. In re Taborsky, 502 F.2d 775, 780, 183 USPQ 50, 55 (CCPA 1974). The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound. In re Stemniski, 444 F.2d 581, 586, 170 USPQ 343, 347 (CCPA 1971), Taborsky, 502 F.2d at 781, 183 USPQ at 55, In re Murch, 464 F.2d 1051, 175 USPQ 89 (CCPA 1972), In re Fay, 347 F.2d 597, 146 USPQ 47 (CCPA 1965).

In Stemniski, the claimed compounds were rejected over structurally closely related compounds disclosed in prior art references. The references did not disclose or suggest any usefulness or significant properties, whereas the applicant disclosed a use for the claimed compounds in his application.

In such a case the court reasoned that the requisite motivation to make the claimed

compounds would not be present. The court doubted whether a prima facie case of obviousness existed:

How can there be obviousness of structure, or particularly of the subject matter as a whole, when no apparent purpose or result is to be achieved, no reason or motivation to be satisfied, upon modifying the reference compounds structure? Where the prior art reference neither discloses nor suggests a utility for certain described compounds, why should it be said that a reference makes obvious to one to ordinary skill in the art an isomer, homolog or analog of related structure, when that mythical, but intensely practical, person knows of no "practical" reason to

make the reference compounds, much less any structurally related compounds?
444 F.2d at 586, 170 USPQ at 347.
Appellants argue that since several utilities were disclosed for the compounds claimed, and Oesterling teaches no significant properties or utility for the disclosed sulfonyl chlorides except as intermediates in the formation of the product sulfonic acids, the rejection of the instant claims is not proper in view of Stemniski. The Patent and Trademark Office (PTO) contends that Stemniski is satisfied and the rejection is proper because Oesterling discloses that the sulfonyl chlorides are used as intermediates or starting materials for producing useful acids.
The PTO further argues that the disclosed utility for the Oesterling sulfonyl chlorides as an intermediate for producing useful acids is a usefulness conforming with statutory guidelines, but cites cases for support which are actually inapposite: Reiners v. Mehltretter, 236 F.2d 418, 421-22, 111 USPQ 97, 100 (CCPA 1956), an interference in which structural obviousness was not an issue, and In re Kirk, 376 F.2d 936, 943-44, 153 USPQ 48, 54 (CCPA 1967), a case dealing with appellant's disclosure of "how to use" the claimed compounds under 35 U.S.C. §112.
Other cases involving obviousness have dealt with the role of intermediates. In In re Gyurik, 596 F.2d 1012, 201 USPQ 552 (CCPA 1979), the claimed thio compounds were rejected as prima facie obvious over a reference which generally disclosed such thio compounds as intermediates in the preparation of the corresponding sulfonyl compounds having the same general properties as those of the claimed compounds. The issue framed by the court was based solely upon the status of the claimed compounds as intermediates in the production of end products specifically named in the prior art.
In reversing the obviousness rejection the court said:
An element in determining obviousness of a new chemical compound is the motivation of one having ordinary skill in the art to make it. That motivation is not abstract, but practical, and is always related to the properties or uses one skilled in the art would expect the compound to have, if made. In re Stemniski * * * * The present obviousness rejection cannot stand without some basis in the expected properties of the claimed compounds.
In obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the prima facie case of obviousness, rises from the expectation that compounds similar in structure will have similar properties. * * * No common-properties presumption rises from the mere occurrence of a claimed compound at an

intermediate point in a conventional reaction yielding a specifically named prior art compound. That an intermediate/end-product relationship exists between a claimed compound and a prior art compound does not *alone* create a common-properties presumption. Absent that presumption or other evidence of motivation, it cannot be said that it would have been obvious to stop the process for synthesizing the disclosed end product and isolate the claimed intermediate.[14] [Citations omitted.]

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[14]The mere ability of a compound to act as an intermediate toward the production of other compounds does not alone constitute the sort of "property" that the cases on obviousness of chemical compounds contemplated.
Id. at 1018, 201 USPQ at 557-8.
The court explained footnote 14 of Gyurik in In re Magerlein, 602 F.2d 366, 373 n.15, 202 USPQ 473 , 479 n.15 (CCPA 1979):
Our recent statement * * * should not be read out of context as suggesting that the capacity to react to produce another compound is not, ipso facto, a property. The statement is merely a recognition that *there is no common-properties presumption or evidence of motivation to make the intermediate from the mere fact that an intermediate is in the chain of production of another compound.* [Emphasis added.]
Although Gyurik was not a case of obviousness based on structural similarity, and the facts of both Gyurik and Magerlein are different from those here, the dicta in those cases is helpful as a guide.
The PTO places great emphasis on the label "useful," contending that because the Oesterling final product is "useful," the intermediate sulfonyl chlorides are also "useful."

That there is no common-properties presumption accorded to an intermediate and the end product of the reaction involving that intermediate necessarily means that there is no presumption that an intermediate's utility would be the same as that of the end product. Even if an unspecified "usefulness" or utility were all Stemniski requires, such utility could not be imputed from the fact that the Oesterling final product is "useful." The use of such labels, however, is meaningless

because we always look to "the subject matter as a whole" in determining whether the subject matter "would have been obvious at the time the invention was made." Further, a relevant property of a compound cannot be ignored in the determination of non-obviousness. In re Papesch, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963).

Ultimately our analysis of the obviousness or nonobviousness of appellants' claimed compounds requires inquiry as to whether there is anything in the Oesterling reference which would suggest the expected properties of the claimed compounds or whether Oesterling discloses any utility for the intermediate sulfonyl chlorides which would support an expectation that the claimed compounds would have similar properties.

[1] There is no disclosure that the Oesterling compounds would have any properties in common with those of appellants' compounds, as those properties of the former relate to the use of the compounds for base neutralization, catalysis, metal cleaning, and fuel. The mere fact that Oesterling's sulfonyl chlorides can be used as intermediates in the production of the corresponding sulfonic acids does not provide adequate motivation for one of ordinary skill in the art to stop the Oesterling synthesis and investigate the intermediate sulfonyl chlorides with an expectation of arriving at appellants' claimed sulfonyl halides for use as corrosion inhibiting agents, surface active agents, or leveling agents.

Oesterling does not teach the isolation and investigation of the intermediate sulfonyl chlorides, but rather discloses, as an optional step, the isolation and purification of the intermediate to obtain a purer sulfonic acid end product. The isolation and subsequent use of the intermediate sulfonyl chlorides in the production of the corresponding useful sulfonic acids is not motivation sufficient to support the structural obviousness rejection. The board has therefore failed to properly establish that the claimed compounds would have been prima facie obvious in view of Oesterling.

The decision of the board affirming the rejection of claims 13-22 is *reversed.*

- End of Case -

In re TABORSKY

(CCPA)
183 USPQ 50

Decided Aug. 29, 1974
No. 9183
U.S. Court of Customs and Patent Appeals

Headnotes

PATENTS

1. Patentability — Invention — In general (§ 51.501)

In determining propriety of Patent Office case for prima facie obviousness, it is necessary to ascertain whether prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making proposed substitution or other modification.

2. Patentability — Composition of matter (§ 51.30)

Claims should not be rejected under 35 U.S.C. 103 where prior art provides one of ordinary skill in the art with no motivation to make proposed molecular modifications needed to arrive at applicant's claimed compounds.

3. Patentability — Composition of matter (§ 51.30)

Since comparative evidence demonstrates that claimed compounds possess biological activities beyond what could reasonably be predicted by person of ordinary skill in the art, it is unnecessary for court to specifically pass on issue of whether these compounds are prima facie obvious since, even if they are, the prima facie case has been overcome by the evidence; compound and its properties are inseparable in patent law.

Particular patents—3-Nitrohalosalicylanilides

Taborsky, 3-Nitrohalosalicylanilides, claims 1 to 8 of application allowed.

Case History and Disposition:

Appeal from Board of Appeals of the Patent Office.

Application for patent of Robert G. Taborsky, Serial No. 730,596, filed May 20, 1968; Patent Office Group 121. From decision rejecting claims 1 to 8, applicant appeals. Reversed.

Attorneys:

ARTHUR L. CAIN and CAIN & LOBO, both of Cleveland, Ohio, for appellant.

JOSEPH F. NAKAMURA (HENRY W. TARRING II of counsel) for Commissioner of Patents.

Judge:

Before MARKEY, Chief Judge, and RICH, BALDWIN, LANE, and MILLER, Associate Judges.

Opinion Text

Opinion By:
LANE, Judge.

This is an appeal from the decision of the

Page 51

Patent Office Board of Appeals, adhered to after reconsideration, which affirmed (with one examiner-in-chief dissenting) the rejection under 35 U.S.C. 103 of claims 1 through 8 in appellant's patent application serial No. 730,596, filed May 20, 1968, [1] for "3-Nitrohalosalicylanilides." We reverse.

Claimed Subject Matter

3-Nitrohalosalicylanilides have the following general structural formula (numerals indicate ring positions):
Graphic material consisting of a chemical formula or diagram set at this point is not available.

See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

In the above structural formula, the left-hand aromatic ring is called the "salicyl" ring and the right-hand aromatic ring is called the "aniline" ring.

Claim 1 is a generic claim to 3-nitrohalosalicylanilides:

> 1. A 3-nitrohalosalicylanilide having the formula
> *Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.*
> where Y is a halogen and n is a positive integer no greater than 5. [2]

Claim 2 is an independent subgeneric claim reciting the structural formula shown in claim 1 where Y is a halogen and n is a positive integer no greater than 3.

Claims 3-8 are dependent on claim 2, and they recite individual chemical species where the identity or the position of the halogen substituent varies as follows:

Claim 3:
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Claim 4:
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

Claim 5:
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Claim 6:
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

Claim 7:
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Claim 8:
Graphic material consisting of a chemical formula or diagram set at this point is not available.

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The remaining claim, independent claim 9 stands allowed:

> 9. A 3-nitrohalosalicylanilide having the formula
> *Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.*

Appellant's specification states that 3-nitrohalosalicylanilides are useful, inter alia, as piscicidal agents for selectively eradicating brown bullhead fish and as selective larvicides for controlling sea lamprey, the latter having caused great damage to commercial fish, such as trout, in the Great Lakes. Data in the specification indicate that several of appellant's claimed compounds possess a significantly greater lethal effect to sea lamprey larvae than to fingerling rainbow trout.

References

The examiner and the board relied on four prior art references:

> (1) Schraufstatter and Gonnert [Schraufstatter], U. S. Patent 3,079,297, granted February 26, 1963 (filed May 31, 1960; claims benefit of earlier applications)
>
> (2) Strufe, Schraufstatter, and Gonnert [Strufe], U. S. Patent 3,113,067, granted December 3, 1963 (filed August 23, 1960)
>
> (3) Ioffe et al. [Ioffe I], Zhurnal Obshchei Khimii, 29:2682-2685 (August 1959)
>
> (4) Ioffe et al. [Ioffe II], Chem. Abstracts, 54:10938 (1960)

The examiner cited another reference, not as prior art, but for the purpose of establishing "certain statements of fact" (relying on In re Wilson, 50 CCPA 773, 311 F.2d 266, 135 USPQ 442 (1962)):

> Howell et al. [Howell], U. S. Patent 3,238,098, granted March 1, 1966 (application filed January 27, 1964) [3]

Appellant cited two references:

> Starkey, U. S. Patent 3,309,267, granted March 14, 1967
>
> Taborsky, U. S. Patent 3,527,865, granted September 8, 1970 [4]

Rejection

The examiner rejected claims 1-8 under 35 U.S.C. 103 as "obvious over" Schraufstatter, Strufe, and the two Ioffe references. The board majority sustained this rejection and stated: "We agree with the examiner that the claimed compounds are *structurally obvious* and that the evidence offered by appellant to show that the compounds have unexpected beneficial properties fails of its objectives." (Emphasis ours.) The dissenting examiner-in-chief would have reversed the rejection because "* * * the art of record fails to establish that the invention, as a whole, would have been obvious to a person having ordinary skill in the art, In re Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (1963)."

Schraufstatter

The Schraufstatter patent, the first prior art reference, is entitled "Method of Combating Gastropods," and it discloses that certain derivatives of 2-hydroxy-benzoic-anilide are effective gastropodicidal agents. Schraufstatter broadly defines a genus of 2-hydroxy-benzoic-anilide derivatives having the following structural formula:
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

> wherein R is hydrogen or a lower alkanoyl radical having from 1 to 4 carbon atoms and which is substituted at one of the numbered positions with a halogen atom and at another numbered position with a member selected from the group consisting of halogen and the nitro group; and further members of *the said first mentioned group* substituted at a total of up to three additional of the numbered positions with members selected from the group consisting of halogen, methyl and trifluoro methyl, the total number of halogen substituents, however, not exceeding four and the total number of nitro groups not exceeding two.
>
> Here and in the following, chlorine, bromine and iodine are to be understood by "halogen." [Emphasis ours.]

This definition of the genus is unclear since the phrase "the said first mentioned group" is ambiguous. Nevertheless, the genus appears to include compounds where R is hydrogen, a halogen "is substituted at one of the numbered positions," and a nitro (-NO_2) group is substituted "at another numbered position." Thus, the defined genus encompasses a large number of compounds, including some of appellant's claimed compounds.

Schraufstatter then defines a subgenus of "particularly active gastropodicidal agents in accordance with the invention" which has the following formula:

Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

> wherein R is hydrogen or a lower alkanoyl radical having from 1 to 4 carbon atoms, R $_1$is hydrogen or methyl, R $_2$is chlorine or bromine, R $_3$and R $_4$are hydrogen, methyl, chlorine or bromine, or a nitro group, R $_4$[sic] and R $_6$are hydrogen, chlorine or bromine and wherein always only one nitro group and at most three halogen substituents are present.

This subgenus does not encompass appellant's claimed compounds since, by definition, only R $_3$and R $_4$may be nitro groups and the structural formula shows that R $_3$and R $_4$are always on the *aniline* ring (the right-hand ring). Appellant's claimed compounds always have the nitro group at the 3 position on the *salicyl* ring (left-hand ring).

Schraufstatter then gives "[b]y way of example" a list of the chemical names and the melting points of twenty specific derivatives of 2-hydroxy-benzoic-anilide said to be "notably useful and more or less readily producible compounds." Inspection of this list reveals that three of the twenty compounds do not contain a nitro group. The other seventeen compounds each contain at least one nitro group (one compound contains two nitro groups). Sixteen of these seventeen compounds have the nitro group(s) located on the *aniline* ring *as required by the sub-genus* , above. One of these seventeen compounds has the nitro group on the *salicyl* ring (the left-hand ring), and that compound is disclosed as follows:

Table set at this point is not available. See table in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

To illustrate, the named prior art compound has the following structural formula:
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

[prior art]

This compound departs from the definition of the sub-genus since it has the nitro group on the *salicyl* ring (the left-hand ring) whereas the sub-genus requires that the nitro group be located on the *aniline* ring.

What remains in Schraufstatter—working examples of how to synthesize eight specific compounds, a table showing minimum concentrations needed to produce a 100% death rate in snails after 24 hours using specific compounds, and a working example of how to prepare compositions consisting of the active ingredient plus a carrier (e.g.—an emulsifier)—is concerned only with compounds which come within the defined sub-genus.

The prior art compound, 5-nitro-4¢ -chlorosalicylanilide, differs structurally from the compound recited in appellant's claim 5 in the position of the nitro group on the salicyl ring. The claim 5 compound has the nitro group at the 3 position of the salicyl ring while the prior art compound has the nitro group at the 5 position of the salicyl ring. Another way of expressing this structural difference is to say that in the claim 5 compound the nitro group is in an adjacent position relative to the hydroxy (-OH) group on the salicyl ring whereas in the prior art compound the nitro group is in the opposite position relative to the hydroxy group on the salicyl ring. In short, the claim 5 compound is structurally a non-adjacent position isomer of the prior art compound.

Strufe

The Strufe patent, the second prior art reference, is entitled "Alkanolamine Salts of Salicyl Anilides And Process For Their Production", and it discloses that alkanolamine salts of salicyl anilides are useful for "combating snails and slugs." The Strufe patent is related to the Schraufstatter patent in that Schraufstatter and Gonnert, the two co-inventors shown in Schraufstatter, are also co-inventors in Strufe, and the two patents indicate a common assignee.

Strufe defines a genus of alkanolamine salts of salicyl anilides as follows:

> Generally the new compounds of this invention are alkanolamine salts of salicyl anilides of the general formula
> *Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.*

> wherein R_1 denotes hydrogen or an aliphatic acyl radical, R_2 and R_3 denote a nitro group, chlorine or bromine whereby at least R_2 and R_3 means a halogen atom, R_4 denotes hydrogen or alkyl or alkoxy groups with 1-5 carbon atoms or nitro groups whereby at least one of R_4 denotes a nitro group.

Strufe teaches that:

> The production of the aforesaid alkanolamine salts is carried out according to known methods by reacting the salicyl anilides with alkanolamines such as a mono-ethanolamine, N-methyl-ethanol-amine or 1,2-dimethyl-ethanolamine and the like.

Strufe expressly refers to Schraufstatter when stating that:

> The free salicyl anilides and their gastropod combating properties are the subject matter of * * * [identifying by serial number the great-grandparent application, the grandparent application, the parent application, and the application which has] issued to

Patent 3,079,297 [the Schraufstatter patent].

Strufe points out a practical disadvantage when using the compounds broadly disclosed by Schraufstatter:

> As it is stated above it is known to use substituted 2-hydroxybenzanilides and their O-acyl compounds as gastropod combating agents; however, these compounds are barely water-soluble and have therefore several disadvantages in practice.

Strufe states that it is known to use substituted 2-hydroxybenzanilides in the form of their alkali metal salts, but that the majority of these compounds have the "disadvantage of being rapidly re-precipitated" in water containing mineral salts, and therefore they are "not very suitable for combating snails living in water."

Having thus described a practical problem confronting those skilled in the art, Strufe indicates that he has solved the problem by producing and using alkanolamine salts of salicyl-anilides "* * * which are not precipitated in an aqueous mineral-salt-containing solution [and] which are stable even without addition of emulsifiers * * *."

Strufe then gives working examples of how to prepare nine specific alkanolamine salts of salicyl anilides. The salicylanilide starting compound in each example is either a 2¢ -nitro-salicylanilide or a 4¢ -nitrosalicylanilide, viz., where the nitro group is substituted on the aniline ring.

Following the working examples is a list of fourteen "[o]ther salicylanilides which can be reacted with suitable alkanolamines to give useful compounds * * *." Among the fourteen compounds is: "5-nitro-4¢ -chlorosalicylanilide (M.P. 252°)."

As in Schraufstatter, this is the sole compound specifically disclosed in the list or in the entire reference where the nitro group is on the salicyl ring, and the chemical name and melting point are the sole disclosures relevant to the compound.

offe I and II

The third and fourth prior art references are Ioffe I and Ioffe II, respectively. Ioffe I is a technical paper entitled "N-Substituted Amides of Salicylic Acid and Its Derivatives. I. Arylides of 3,5-Dichlorosalicylic and 5-Nitrosalicyclic Acids.", translated from a Russian chemical journal. Ioffe II is cumulative to Ioffe I since Ioffe II is the abstract of Ioffe I published in Chemical Abstracts.

Ioffe I is mainly concerned with methods of chemical synthesis, and the authors conclude that the best method of preparing arylides of salicylic acid is by "the direct alloying of salol [phenyl salicylate] with amines." They state that the derivatives produced by their "salol method" are "more pure" than the same derivatives when prepared by reacting a substituted-salicylic acid with a substituted-amine in the presence of phosphorus trichloride. Ioffe I presents tables showing twelve specific derivatives of 3,5-dichlorosalicylic acid and the corresponding twelve specific

derivatives of 5-nitrosalicylic acid. Among the twelve derivatives of 5-nitrosalicylic acid is the following compound:

Table set at this point is not available. See table in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

Hence, Ioffe I discloses the same compound, 5-nitro-4¢ -chlorosalicylanilide, shown by Schraufstatter and Strufe. The examiner recognized that Ioffe I was cumulative to Schraufstatter and Strufe, and stated that Ioffe I "was cited because of its date." Ioffe I does not disclose any biological utility for this compound or for any derivative of 5-nitrosalicylic acid. Ioffe I only states that: "In reduction, the arylides of the 5-nitrosalicylic acid are transformed into corresponding arylides of the 5-amino-salicylic acid, which are diazotized and form azo dyes together with azocomponents."

Opinion

The general issue is whether the cited prior art established that "* * * the *differences* between the subject matter sought to be patented and the prior art are such that the subject matter *as a whole* would have been obvious *at the time the invention was made* to a person having ordinary skill in the art * * *." 35 U.S.C. 103 (emphasis ours). The specific issues are

whether appellant's claimed chemical compounds are prima facie obvious because of structural similarity to the cited prior art and, if so, whether there is a sufficient showing to rebut prima facie obviousness.

Fluoro-Substituted Compounds

With respect to the compounds recited in claims 1 and 2 when Y is fluorine and with respect to the compound 3-nitro-4-fluorosalicylanilide recited in claim 6, we hold that the cited prior art fails to establish prima facie obviousness. To arrive at these fluoro-substituted compounds, one must modify the closest prior art compound, 5-nitro-4-chlorosalicylanilide, in two essential ways, first by changing the position of the nitro group from the 5 position to the 3 position, and second, by changing the identity of the halo-substituent from chloro to fluoro.

[1] In determining the propriety of the Patent Office case for prima facie obviousness, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the proposed substitution or other modification. In re Lintner, 59 CCPA 1004, 1007, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (1972).

[2] Schraufstatter expressly limits the scope of "halogen" in the definition of his genus to "chlorine, bromine, and iodine." Thus, appellant's fluoro-substituted compounds are outside Schraufstatter's genus as well as Schraufstatter's sub-genus. Strufe's reference to "[t]he free salicyl anilides" of Schraufstatter similarly limits the disclosure of Strufe to "chlorine, bromine,

and iodine." Furthermore, Strufe as a whole is directed to preparing alkanolamine salts of salicylanilides because, as he states it, free salicylanilides have "several disadvantages in practice." Ioffe I does not mention or suggest the desirability of any fluoro-substituted compounds. In short, the prior art of record provides one of ordinary skill in the art with no motivation to make the proposed molecular modifications needed to arrive at appellant's claimed fluoro-substituted compounds. See In re Murch, 59 CCPA 1277, 464 F.2d 1051, 175 USPQ 89 (1972), and In re Fay, 52 CCPA 1483, 347 F.2d 597, 146 USPQ 47 (1965). The questions posed by this court in In re Stemniski, 58 CCPA 1410, 1416, 444 F.2d 581, 586, 170 USPQ 343, 347 (1971), are also relevant here:

> * * * what on this record—other than abstract, theoretical or academic considerations—would lead one of ordinary skill to change the structure of the reference compounds to obtain the claimed compounds? Certainly no practical considerations which promote the progress of useful arts or are of use to society are manifest. How can there be obviousness of structure, or particularly of the subject matter as a whole, when no apparent purpose or result is to be achieved, no reason or motivation to be satisfied, upon modifying the reference compounds' structure? * * *

Since we hold that the prior art of record fails to establish that the fluoro-substituted compounds recited in appellant's claims are prima facie obvious, it is unnecessary to consider any comparative evidence with respect to the properties of these compounds.

Chloro-, Bromo-, and Iodo-Substituted Compounds

With respect to the compounds recited in claims 1 and 2 when Y is chlorine, bromine, or iodine and with respect to the specific compounds recited in claims 3, 4, 5, 7 and 8, we hold that objective comparative evidence of record establishes the non-obviousness of these compounds. In re Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (1963); In re Wiechert, 54 CCPA 957, 370 F.2d 927, 152 USPQ 247 (1967); Commissioner of Patents v. Deutsche Gold-und-Silver-Scheideanstalt Vormals Roessler, 397 F.2d 656, 157 USPQ 549 (D.C. Cir. 1968); National Distillers & Chemical Corp. v. Ladd, 233 F.Supp. 917, 143 USPQ 59 (D. D.C. 1964).

[3] Since comparative evidence demonstrates that these compounds possess biological activities which are beyond what could reasonably be predicted by the person of ordinary skill in the art, it is unnecessary for us to specifically pass on the issue of whether these compounds are prima facie obvious since, even if they are, the prima facie case has been overcome by the evidence. In re Blondel, 499 F.2d 1311, 182 USPQ 294 (CCPA 1974).

We begin our review of the comparative evidence of record with the claimed compound 3-nitro-4-chlorosalicylanilide (claim 5), which is a non-adjacent position isomer of the prior art compound 5-nitro-4-chlorosalicylanilide disclosed by Schraufstatter, Strufe and Ioffe I. The Howell patent, which was cited by the examiner (although not a prior art reference) and by appellant (to show unexpected properties), indicates in Table V that the claimed compound

produces 100% mortality in sea lamprey larvae at a low concentration of 0.3 parts per million of water. Comparative data for the prior art compound 5-nitro-4-chlorosalicylanilide is found in Howell's Table IV where it is indicated that a higher concentration of 0.5 parts per million is necessary to produce 100% mortality in sea lamprey larvae.

Such an objective difference in the desired toxicity of the claimed compound is unexpected in view of the seemingly minor difference

in molecular structure, and that difference in toxicity is an empirical fact which could not be reasonably predicted by one of ordinary skill in the art. Hence, the difference in toxicity is persuasive evidence that the claimed compound has non-obvious properties. Since a compound and its properties are inseparable in patent law, In re Papesch, supra, "* * * the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would [not] have been obvious at the time the invention was made to a person having ordinary skill in the art * * *." 35 U.S.C. 103.

Similarly, Howell teaches that 3-nitro-4-bromosalicylanilide (claim 8) produces 100% mortality in sea lamprey larvae at a concentration of 0.3 parts per million while the corresponding compound 5-nitro-4- bromosalicylanilide (not specifically disclosed in the prior art) requires a higher concentration of 0.5 parts per million to produce 100% mortality. Appellant's specification states that 3-nitro-4-iodosalicylanilide (claim 7) produces 100% mortality in sea lamprey larvae at a concentration of 0.3 parts per million while Howell states that the corresponding compound 5-nitro-4-iodosalicylanilide (not specifically disclosed in the prior art) requires a higher concentration of 0.5 parts per million to produce 100% mortality.

Furthermore, Howell states that 3-nitro-3-chlorosalicylanilide (claim 4) produces 100% mortality in sea lamprey larvae at a concentration of 0.3 parts per million while the corresponding compound 5-nitro-3-chlorosalicylanilide (not specifically disclosed in the prior art) requires the higher concentration of 15.0 parts per million to produce 100% mortality.

We conclude that the objective evidence, comparing representative claimed compounds with the corresponding 5-nitro compounds, is sufficient to establish differences which demonstrate the nonobviousness of all of appellant's claimed chloro-, bromo-, and iodo-substituted compounds.

The decision of the board is *reversed.*

Footnotes

Footnote 1. This application is a continuation-in-part of application serial No. 469,300, filed July 2, 1965, which in turn was a continuation-in-part of application serial No. 325,473, filed November 21, 1963, and application serial No. 435,686, filed February 26, 1965, which were

both filed as continuations-in-part of application serial No. 56,679, filed September 19, 1960.

Footnote 2. The structural formulas in appellant's claims depict the compounds as containing six-membered *aliphatic* rings. However, it is clear from the chemical name 3-nitrohalosalicylanilide that appellant intends to claim compounds which contain six-membered *aromatic* rings. The examiner has advised appellant that he will be required to indicate that the rings in the structural formulas are aromatic.

Footnote 3. The Howell patent (assigned to the United States of America as represented by the Secretary of the Interior) was involved in an interference with Taborsky's application serial No. 539,723, filed April 4, 1966, as a division of application serial No. 469,300, see note 1, supra. Taborsky was the successful party. See Howell v. Taborsky, 164 USPQ 58 (Bd. Pat. Intf. 1969).

Footnote 4. This patent was granted on application serial No. 539,723, see note 3 supra.

- End of Case -

